MAR 29 1911

VOL. CXLI, NO. 4 APRIL, 1911 NO. 469

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

EDITED BY A. O. J. KELLY, M.D.

THE THERAPEUTICS OF DIGITALIS AND ITS ALLIES. By ARTHUR R. CUSHNY, M.D., F.R.S. 469

PERSONAL EXPERIENCES WITH THE USE OF SALVARSAN (DIOXYDIAMIDOARSENOBENZOL, OR "606") IN THE TREATMENT OF SYPHILIS. By HERMANN GOLDENBERG, M.D., and DAVID J. KALISKI, M.D. 485

THE PHYSIOLOGY OF THE PITUITARY GLAND AND THE ACTIONS OF ITS EXTRACTS. By CARL J. WIGGERS, M.D. 502

STIFF AND PAINFUL SHOULDERS, WITH LOSS OF POWER IN THE UPPER EXTREMITY. By T. TURNER THOMAS, M.D. 515

THE INTERRELATION OF THE ORGANS OF INTERNAL SECRETION. By R. G. HOSKINS, Ph.D. 535

THE SUDDEN ONSET OF PARALYSIS IN POTT'S DISEASE WITHOUT DEFORMITY OF THE VERTEBRÆ. By WILLIAMS B. CADWALADER, M.D. 546

THE PATHOLOGICAL FINDINGS IN THE PARATHYROIDS IN A CASE OF INFANTILE TETANY. By B. S. OPPENHEIMER, M.D. 558

SARCOMA OF THE VAGINA. By JOSEPH McFARLAND, M.D. 570

PROGNOSIS OF TUBERCULOUS LESIONS INVOLVING THE WHOLE OF OR MORE THAN ONE LOBE. By JOSEPH WALSH, M.D. 589

PHILADELPHIA AND NEW YORK
LEA & FEBIGER

COPYRIGHT 1911, BY LEA & FEBIGER. ALL RIGHTS RESERVED. ENTERED AT THE POST-OFFICE AT PHILADELPHIA AS SECOND-CLASS MATTER

PUBLISHED MONTHLY. SUBSCRIPTION, FIVE DOLLARS A YEAR, POSTPAID

IMPORTANT ANNOUNCEMENT.

New (3d) Edition **Just Ready** **Thoroughly Revised**

THE DISEASES OF THE

NOSE, THROAT AND EAR

MEDICAL AND SURGICAL.

By WILLIAM LINCOLN BALLENGER, M.D.

Prof. of Otology, Rhinology and Laryngology, College of Physicians & Surgeons, Chicago

Octavo, 983 pages, 506 engravings, mostly original, and 22 plates. Cloth, $5.50 net

The phenomenal demand for three large editions of this work in much less than three years is explained by its combination of utility, completeness and high authority. Professor Ballenger began by procuring all the latest literature, embracing some 3,000 monographs, pamphlets and reprints, the smaller items being particularly valuable because announcements of advances are naturally made in journal articles. Thus he covered the knowledge of the whole world and made his book cosmopolitan in scope. His mastery of the field enabled him to present the best methods of treatment yet evolved. With equal disregard of labor and expense he produced a profusion of original and effective drawings, illustrating even the steps of operations, so that his readers could master the technique at leisure. It is not to be wondered at that a book of such authority and practical instructiveness should have received the acclaim of instant and sustained demand, covering as it does important cognate specialties and presenting them in a form suitable for students, practitioners and specialists. Its contents are very comprehensive, as they cover the medical as well as the surgical treatment of the diseases in the entire region of the nose, throat and ear. The rapid succession of editions gave Professor Ballenger's work the further pre-eminent advantage of frequent revisions, this new one being, like its predecessors, revised to the latest date in its text and improved with many new engravings and plates. The volume is, in a word, a combined text-book and atlas of the highest authority, covering its three subjects in the light of the world's most advanced knowledge.

The American Journal of the Medical Sciences.

The respective subjects of the diseases of the nose, throat and ear are all considered with a thoroughness and detail which fully justifies the author's statement in his preface, that the volume may be characterized as a "combined text-book and atlas, covering its three subjects." Dr. Ballenger's descriptions of operative procedures are especially notable for their conciseness and lucidity, and are accompanied by pictures which thoroughly illustrate all the details of the operation. The work may be thoroughly commended as suitable for purposes not only of the student and practitioner, but also of the specialist.

The Journal of Ophthalmology and Otolaryngology.

This work is one of unusual scope and thoroughness. One of its characteristic features is the directness with which the author brings out the practical side of every problem under discussion. The illustrations are unusual in both number and quality. The operative procedures are clearly described, and in many instances the different steps are so well illustrated that one who has never seen some of the operations may undertake them with fair prospect of success. The reviewer believes this is the best work on the subject in the English language, and that a new standard of excellence in this field of literature has been established.

PHILADELPHIA
706-8-10 SANSOM ST.

LEA & FEBIGER

NEW YORK

ed

go

n.
o
e
e
t
l
s

CONTENTS.

ORIGINAL ARTICLES.

The Therapeutics of Digitalis and its Allies 469

By Arthur R. Cushny, M.D., F.R.S., Professor of Pharmacology in the University of London, England.

Personal Experiences with the Use of Salvarsan (Dioxydiamidoarsenobenzol, or "606") in the Treatment of Syphilis 485

By Hermann Goldenberg, M.D., Attending Dermatologist to the Mount Sinai Hospital, and David J. Kaliski, M.D., Assistant in Serum Research, Mount Sinai Hospital, and Assistant in Genito-urinary Diseases in the Mount Sinai Hospital Dispensary, New York.

The Physiology of the Pituitary Gland and the Actions of its Extracts . . 502

By Carl J. Wiggers, M.D., Instructor in Physiology in the University of Michigan, Ann Arbor.

Stiff and Painful Shoulders, with Loss of Power in the Upper Extremity . 515

By T. Turner Thomas, M.D., Associate in Surgery in the University of Pennsylvania; Surgeon to the Philadelphia General Hospital, and Assistant Surgeon to the University Hospital, Philadelphia.

The Interrelation of the Organs of Internal Secretion 535

By R. G. Hoskins, Ph.D., Professor of Physiology in the Starling-Ohio Medical College, Columbus.

The Sudden Onset of Paralysis in Pott's Disease without Deformity of the Vertebræ 546

By Williams B. Cadwalader, M.D., Pathologist to the Orthopædic Hospital and Infirmary for Nervous Diseases; Assistant Instructor in Clinical Neurology and Neuropathology at the University of Pennsylvania, Philadelphia.

The Pathological Findings in the Parathyroids in a Case of Infantile Tetany 558

By B. S. Oppenheimer, M.D., Assistant Physician to the Dispensary of Mt. Sinai Hospital, New York.

Sarcoma of the Vagina 570

By Joseph McFarland, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College, Philadelphia.

Prognosis of Tuberculous Lesions Involving the Whole of or More than One Lobe 589

By Joseph Walsh, M.D., Visiting Physician to White Haven Sanatorium and Consulting Physician to Tuberculosis Department of the Philadelphia General Hospital, Philadelphia.

REVIEWS.

The Expectation of Life of the Consumptive After Sanatorium Treatment. By N. D. Bardswell, M.D., M.R.C.P., F.R.S. 594
An Anatomical and Surgical Study of Fractures of the Lower End of the Humerus. By Astley P. C. Ashhurst, M.D. 594
Pulmonary Tuberculosis and Sanatorium Treatment. By C. Muthu, M.D., M.R.C.S., L.R.C.P. 595
The Principles of Gynecology. By W. Blair Bell, B.S., M.D. 596
Nephrocoloptosis. A Description of the Nephrocolic Ligament and its Action in the Causation of Nephroptosis, with the Technique of the Operation of Nephrocolopexy, in Which the Nephrocolic Ligament is Utilized to Immobilize Both Kidney and Bowel. By H. W. Longyear, M.D. 597
Klinische und Anatomische Beiträge zur Lehre vom Uterusmyom. Von Dr. Med. Anton Garkish 598

PROGRESS OF MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D., AND W. S. THAYER, M.D.

An Early Sign of Aortic Sclerosis 599
Autoserotherapy in Serofibrinous Pleurisy 599
A New Test for Cancer of the Stomach and the Tryptophan Test . . 600
Lipemia in Diabetes 600
Intrathoracic Struma 600
Intravenous and Subcutaneous Administration of Dextrose 601
Generalized Syphilitic Infection of Babbits 601
The Bearing of Old and New Facts Upon Our Conceptions of Cardiovascular Disease 602
On Chylous and Pseudochylous Ascites 603

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D., AND T. TURNER THOMAS, M.D.

The Origin and Treatment of Ischemic Contracture and Gangrene . . . 604
Calculous Anuria in a Case of Single Kidney, Treated and Cured by Ureteral Catheterism 605
A New Gastrostomy Operation 606
Ligation of the Vein in Portal Thrombosis from Appendicitis 606

Making a New Circulation for an Obstructed Circulation in the Abdomen and Lower Extremities 607
Operative Mobilization of the Upper Jaw in Cleft Palate 607
Anesthesia by the Intratracheal Insufflation of Air and Ether. A Description of the Technique of the Method and of a Portable Apparatus for Use in Man 608

THERAPEUTICS.

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

Salvarsan in Syphilis 609
Experimental Studies of the Lethal Dose of Salvarsan in Acid Solution . 609
Atropine Cure in Ulcer of the Stomach, and other Indications for Atropine in Internal Medicine 609
The Prevention of Typhoid Fever with Antityphoid Vaccine 610
The New Preparation of Albumin, "Riba" 610
Subcutaneous and Intravenous Feeding with Glucose 610
Sabromin in Chorea 611
Experimental and Clinical Observations of the Action of Salvarsan on the Eye 611
Antityphoid Inoculation 611
The Effect of Salvarsan upon Cranial Nerves 611
Treatment of Banti's Disease 612

PEDIATRICS.

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.

Serum Treatment on Diphtheria 613
Chorea Successfully Treated with Salvarsan 614
Neurasthenia in Children 614
Some Points on "Serum Disease" 615

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.

Cesarean Section for Impassable Contraction Ring 616
Cesarean Section Under Local Anesthesia 618

GYNECOLOGY.

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.

A New Method of Replacing the Retroflexed Uterus 619
Arteriosclerosis of the Uterine Vessels 619
The Utilization of the Anterior Cervical Wall in the Operation for Vesico-vaginal Fistula 619
An Experimental Study of Ascending Genital Tuberculosis 620
Active Substances in the Uterus and Ovary 620
Some Observations on the Operation of Abdominal Myomectomy for Myomata of the Uterus 620
Carcinoma of the Uterus 621
Epidural Injections in Sacral Pains 621

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

WARFIELD T. LONGCOPE, M.D.

The Relative Importance of the Bovine and Human Types of Tubercle Bacilli in the Different Forms of Human Tuberculosis 622
The Presence of a Diastatic Ferment in Leukocytes 623
The Action of Diuretics upon Diseased Kidneys 623

CLB242542

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES.

APRIL, 1911.

ORIGINAL ARTICLES.

THE THERAPEUTICS OF DIGITALIS AND ITS ALLIES.[1]

By Arthur R. Cushny, M.D., F.R.S.,
PROFESSOR OF PHARMACOLOGY IN THE UNIVERSITY OF LONDON, ENGLAND.

In 1775, William Withering, a Birmingham physician, had his attention drawn to a family receipt for the cure of dropsy long kept secret by an old woman in Shropshire; he found it composed of some twenty herbs, of which he concluded that foxglove was the essential one. After trying it in his practice for some months he "ventured to assert" that this herb "merited more attention than modern practice bestowed on it." These were the days of deliberate observation in medicine however, and it was not until after ten years careful use of it in his practice that he gave his results to the world,[2] although he had induced many of his friends to use it in the meantime. In his "account of the foxglove," he recognizes its action on the heart,[3] but is chiefly interested in its diuretic effects, and does not associate the latter with the cardiac changes. Withering's work directed immediate attention to the new remedy; I find it given an assured place by Barton, of Philadelphia, in 1798. But its true sphere of action was obscured by its being recommended as a cure for phthisis, although its dis-

[1] An address delivered before the Harvey Society of New York, January 14, 1911.

[2] An account of the foxglove, and some of its medical uses with practical remarks on dropsy and other diseases. By William Withering, M.D., Birmingham, 1785. This work bears the appropriate motto *nonumque prematur in annum*, and ought to receive attention as an example of the careful observation of the time; it may be added that it may help to dispel some of the apprehensions of the "cumulative" and other dangerous effects of digitalis which are too prevalent.

[3] "It has a power over the motion of the heart to a degree yet unobserved in any other medicine and this power may be converted to salutary ends," p. 192.

coverer denied it any usefulness in this disease from the beginning. Later it slowly resumed its position as the cardiac remedy par excellence, but curiously enough not as a cardiac tonic, but as a depressant. Sixty years after its introduction into regular medicine Pereira, the great authority of his day, recommended it chiefly "to reduce the force and velocity of the circulation" as in aneurysm and hemorrhage of internal organs. In his time the new method of experimental investigation of the effects of drugs on animals was in its infancy, but it was soon afterward applied to digitalis by Traube, Schmiedeberg, and others, and the action of digitalis and its allies on the organism was ascertained with certainty in many respects, although it still requires further elucidation. The knowledge of its therapeutic use has also advanced since Pereira's time, and few would venture to recommend digitalis in hemorrhage and still fewer in aneurysm at the present time. But this advance in the therapeutic applications has scarcely kept pace with that of the experimental investigation. Too often the diagnosis of cardiac abnormality, the discovery of a murmur, is regarded as an immediate indication for digitalis, so that in the narrower sphere of the circulatory diseases, digitalis suffers today from the same over-appreciation as was its fate a hundred years ago, when to some minds it appeared to be a panacea for all internal disorders. The advance in the diagnosis of heart disease in recent years, however, gives hope that the sphere of action of digitalis may be more circumscribed, and that we may soon reach a point where instead of "trying digitalis" in every case of heart disease we may be able to define the symptom complex which indicates its exhibition as accurately as that for quinine.

It has long been my feeling that the study of experimental pharmacology should be merely the preliminary to investigation in therapeutics, and I very gladly accepted the invitation of my friend Dr. James Mackenzie to associate myself with him in his clinical researches on the effects of drugs on the circulation. Our final object is to differentiate the types of heart disease in which digitalis is useful, and I may say at once that some progress has been made in this direction. Incidentally we have carefully noted the effect of digitalis and its allies on the human heart and circulation with the view that one or the other might be preferable in certain conditions. We are still far from achieving our goal, but a certain amount of information has been acquired, and when your president did me the honor of asking me to address you, I thought that nothing I could offer would be more appropriate to a society that honors the great name of Harvey than a contribution to the therapeutics of the great remedy in diseases of the circulation.

In the experimental laboratory it is found that digitalis affects the heart in several different directions. In the first place, it was recognized early by Traube that the heart is slowed by stimula-

tion of the inhibitory centre in the medulla. Since his time inhibition of the heart has been shown to depress not only the rate, but also the strength of contraction, the conductivity and the tone of the muscle, so that these must be taken into consideration in any account of the changes induced by the drug. On the other hand, digitalis acting directly on the heart muscle increases the strength of contraction, the tone and the excitability. Its direct effects on conductivity have not been accurately determined. The effects of digitalis on the mammalian heart are, therefore, compounded of two influences which in most instances oppose each other. The rhythm is slowed by the inhibition and accelerated by the muscular action, but in moderate quantities in animals the former prevails and the rhythm is slower. The strength of contraction and the tone are reduced by the inhibitory stimulation and increased by the direct action on the heart, and the changes observed are the resultant of these two; in the ventricle the muscular effect prevails and the chamber beats more strongly, and at any rate, in the dilated heart, relaxes less than before the administration. In the auricle, the inhibitory prevails over the muscular factor, and the result is a decrease in the strength of contraction very often, or it may be there is little change to be noted in this chamber from digitalis. In animals the blood pressure rises from contraction of the arterioles which are acted on directly by the glucosides.

In these experiments in animals, the drugs are injected intravenously in order to elicit the effects quickly enough to permit of their being observed within the limits of an experiment of at most three to four hours' duration. In the therapeutic use of digitalis, however, one seldom sees much change from the drug under thirty-six to forty-eight hours. In addition, the dose given experimentally is often very much larger in proportion than that in therapeutic use, and this, together with the rapidity with which it is thrown into the circulation, must cause a much greater concentration in the blood than is induced in therapeutics. Great caution must, therefore, be used in applying the results obtained experimentally in therapeutics, and perhaps this has not been sufficiently appreciated; I cannot cast a stone at any one. But these experimental investigations, at any rate, show that inhibition and muscular action may be elicited in animals by this series, and encourage us to look for these effects in man.

In Dr. Mackenzie's clinic the patients are, of course, examined by his well-known methods, and the course of the disease and the effects of treatment are constantly controlled by graphic tracings in addition to the ordinary clinical notes. Conclusions may, therefore, be drawn with some confidence from a small number of cases. The disorders of the heart were all of such seriousness as to necessitate admission to hospital and detention there, often

for months at a time. The treatment with digitalis was almost always preceded by rest in bed for a week or more in order to eliminate as far as possible the error of attributing to the drug changes really due to the general conditions. The disorders of the heart on which we have made our observations, may be conveniently thrown into two great groups: (1) Those in which the dominant rhythm of the heart continued to originate in the normal point (Keith-Flack node), and (2) those in which the rhythmogenic function was usurped by some other part of the heart, in our cases by the auricle. The effects of digitalis are so different in these two groups that I shall describe them separately.

In the first group digitalis often caused considerable improvement in the general condition, manifested in relief of the dyspnœa or dropsy, or lessened cyanosis, though the benefit was much less obvious than in the second group of cases. This improvement in the general condition was sometimes accompanied by moderate slowing of the pulse which fell from 90 to 110, to 70 to 80 per minute. But this is by no means elicited in every case even when the other symptoms are relieved. Thus, of 18 patients of the first group, only 6 showed any slowing under digitalis, and in one of these it may be questioned whether this was due to the drug. We can safely say that the pulse was slowed by digitalis in only about 30 per cent. of the cases in which the dominant rhythm was of normal origin. In 2 of our 6 cases, the pulse was previously very rapid and it is possible that excessive activity of the rhythmogenic node may favor this effect of digitalis; on the other hand, if this excessive activity arises from fever digitalis often fails to induce slowing. In the other cases in which slowing followed the use of digitalis no feature was observable which distinguished them from those in which no such effect occurred. During the slowing the heart beat continued to bear its ordinary character; in other words, the slowing is due to fewer impulses being emitted by the rhythmogenic area.

The slowing of the heart under digitalis is universally attributed to stimulation of the inhibitory centre in the medulla oblongata, and in fact it bears every resemblance to the effects of such stimulation. Thus the slowing is not uniform, the rhythm varying with the phases of respiration, as it does in normal individuals with marked inhibition. And this respiratory variation may be developed under digitalis in persons in whom it is previously absent or hardly perceptible. Owing to the development of this feature, the intervals between successive pulse beats may show larger variations after digitalis than before, as Wenckebach has recently pointed out, although perhaps his description tends to exaggerate the significance of this feature.

Further evidence that the slowing is inhibitory in origin is offered by the observation that it disappears under doses of atropine which

have no further effect than to prevent the inhibitory impulses reaching the heart. And finally it has been noted that in complete block, digitalis does not slow the ventricle as might be expected if it retarded the heart by direct action on the ventricular muscle, while the auricle continues to be slowed as in the normal heart.

The question arises why digitalis fails in so many instances to slow the heart. We may exclude at once inactivity of the drug because our preparations were assayed pharmacologically and on treating two patients with the same tincture in the same doses, the one may respond by marked slowing, while the other shows no such effect even when the drug is pushed until nausea and vomiting are produced. Either the centre in the medulla is incapable of stimulation in these recalcitrant cases, or it is incapable of holding the heart in check. It is known that the control ordinarily exercised by the inhibitory centre over the heart varies in different individuals and at different ages in the same individual, and evidence is not wanting that the resistance of the heart to the maximal activity of the centre also varies in the same way. In many instances this resistance is great enough to render nugatory the increased activity of the inhibition induced by digitalis; this resistance to inhibition is especially marked in cases of fever, more particularly when the infection is located in the heart muscle itself as in active myocarditis, in which the irritability of the heart must be considered abnormally augumented.

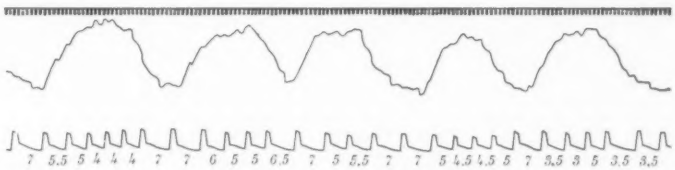

FIG. 1.—Tracing of the respiration (upper) and radial pulse (lower) in patient under digitalis, showing sinus arrythmia.

When digitalis is pushed further in susceptible cases, the inhibition becomes more marked, and obvious irregularities may appear. One of these, like the general slowing, arises from inhibition of the rhythmogenic area—the sinus irregularity, as it has been called. It often occurs without drugs, and consists in alternate phases of slowing and quickening of the heart corresponding to the inspiration and expiration, and is generally attributed to the inhibitory cardiac centre being involved in the stimulation of the respiratory centre; the stimulus is said to spread to the inhibitory centre. The sinus irregularity of digitalis is sometimes of the same kind, the slowing and quickening corresponding to the movements of respiration fairly closely (Fig. 1). In most cases, however,

this does not hold, the phase of slowing recurring at intervals which are much longer than those of respiration. Here one may suppose that the excited inhibitory centre is aroused by stimuli radiating from some other centre than the respiratory, perhaps from the vasomotor area. In any case, in this sinus slowing, as in the regular slowing, the contractions of the heart are normal in character, the only departure being a slower generation of impulses by the rhythmogenic centre. I have already mentioned that careful measurements show that in the ordinary slowing from digitalis variations in the rhythm corresponding to the respiration are present. The sinus irregularity is merely an exaggerated form of this induced by larger doses of the drug in susceptible cases.

In other instances in which digitalis is pushed, an irregularity of another kind is developed; the impulses are generated regularly, but fail to reach the ventricle owing to their not being transmitted along the bundle of His. There is, in fact, a partial heart block. The features of this condition have been so fully discussed of late years that it is unnecessary to describe them here. You know how the auricle continues to beat regularly, but every now and then an impulse fails to reach the ventricle and a pulse beat is

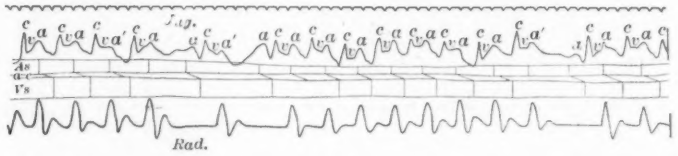

FIG. 2.—Tracing of jugular (upper) and radial pulse (lower) in patient under digitalis, showing occasional failure of the ventricle to contract; a diagram is interposed showing this more clearly. (Mackenzie.)

dropped. This has been noted by a number of observers in the use of digitalis, and has generally been ascribed to the conduction of the bundle having been reduced by the inbibitory stimulation of the drug. It appears to occur especially in cases in which the transmission of impulses is already impaired by disease, as is indicated by the interval between the auricular and ventricular contraction being much prolonged, but it may be induced by digitalis when no impairment of conductivity was detected before; while on the other hand, Mackenzie gives a case in which the conduction was very slow before digitalis, and did not seem to be further depressed by it. This failure of conduction from the auricle to the ventricle under digitalis is universally ascribed to the inhibitory action of the drug, and in fact, has been seen to disappear under atropine, which removes the inhibitory action of the cardiac vagus. This may seem proof positive and I am not prepared to deny that in these cases the inhibition is the potent

factor in the irregularity. At the same time, I am not satisfied that it is the only one; for in animal experiments I have seen repeatedly, in fact it is the general rule at a certain phase of the action, that complete block is elicited, the auricles and ventricles beating independently, and yet this block is independent of the inhibitory action for it occurs after large doses of atropine. I should not be surprised to find that in man also the conductivity of the bundle is impaired by direct action on it and the further lowering of its activity by the inhibitory factor induces the block with which we are all familiar. This irregularity is often accentuated at certain phases of the respiration at which the constant inhibitory influence of the drug is reinforced by the stimulus radiating from the respiratory centre.

These two irregularities from excessive inhibition may occur spontaneously in treatment with digitalis. When they are not present, they may sometimes be elicited by further stimulation of the inhibitory mechanism, direct or reflex. Thus slight pressure on the vagus nerve in the neck is often sufficient to demonstrate this action under digitalis. Latent irregularity may also be discovered in some patients by giving them water to sip. Each time

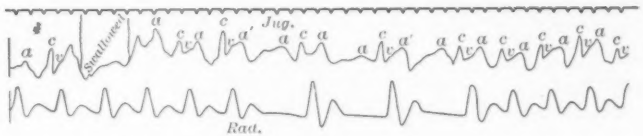

FIG. 3.—Tracing of jugular (upper) and radial pulse (lower) under digitalis in which the rhythm is ordinarily regular, but in which partial block is induced by swallowing. (Mackenzie.)

water is swallowed the pulse is remarkably slowed and either sinus arrhythmia or partial block occurs. Here, I presume, the excitation of the centres governing swallowing radiates to the centre for cardiac inhibition and arouses it to excessive action. As a measure of the recovery of our patients, we often send them up a flight of stairs and then record the pulse rate immediately afterwards. In a number of cases we have noted that the slowing which follows the initial acceleration of the pulse, went on to irregularity, either sinus or block according to the case; in these there was no irregularity except after this slight exertion.

There can, therefore, be little question that the action of digitalis on the inhibitory mechanism which has been investigated in animals, is exerted in a very similar way in a certain proportion of human patients treated with this drug. In moderate degree the inhibition effect slows the pulse, in larger development it may lead to irregularities or, at any rate, favor their development. The sinus

irregularity and the partial block are always preceded and accompanied by slowing. All three features may be developed in the same patient, the sinus irregularity occurring at one time and block at another.[4] I may add that I elicited and described the phenomena now known as sinus arrhythmia and block by digitalis in the dog many years ago and demonstrated that they were inhibitory in nature. That they occur on stimulation of the vagus in animals is common knowledge.

When we come to look for evidence of the direct action of digitalis on the heart muscle in these cases the position is a much more difficult one, for our present methods of heart examination give very inadequate information of changes in the contractility and tone. I may remark in passing, that here history is repeating itself, for direct proof of the inhibitory action of digitalis was available in experimental investigations on mammals many years before it could be shown to act on the muscle directly. The essential feature of digitalis action in animals in small doses is the stronger beat of the ventricle. In patients, this is difficult to demonstrate. It is true that the apex beat may be considered stronger and the pulse beat larger, but no method of measuring these satisfactorily has yet been devised. And even if this were possible, another difficulty has to be faced; for the heart is often slower, and this in itself would tend to strengthen the contraction of the heart and would increase the stroke of the pulse. So that it is impossible at present to demonstrate directly that the contractility of the heart muscle is increased. Another feature observed in animals experimentally is the lessened relaxation in dilated hearts, and there seemed some hope that this might be demonstrable clinically. But in a number of cases in which we attempted to satisfy ourselves on this point, we could make out no change in the area of cardiac dulness, even when digitalis improved the general condition quite satisfactorily. And the apex beat did not move inward. I do not deny that in some cases these alterations in the physical signs are observable, but in our experience such a change is not by any means always apparent, even when digitalis is exercising its full beneficial effects. In a certain number of cases, however, indirect evidence of the action on the heart muscle may be offered. Thus in a number of patients digitalis failed to reduce the pulse rate or to induce any symptom which could be ascribed to the inhibition; yet in these cases, the embarrassment of the breathing became less, anasarca disappeared and the general condition seemed

[4] The fact that the slowing, the sinus arrhythmia and block are so frequently seen together while the last two arise from different parts of the heart, suggests that in these patients the abnormality consists in unusual sensitiveness of the inhibitory centre rather than in a low degree of resistance of the heart to inhibition. For there is no reason why both the rhythmogenic centre and the bundle of His should so often show the same variations. And this would imply that the absence of slowing in most cases is due to failure of the inhibitory centre to react to the drug.

improved, and this relief must, therefore, be attributed to the only other factor which we know—the muscular action. Similarly, in some cases in which helleborein was given (in ½-grain doses t. d. s.), the pulse was not slowed, and no other symptom of inhibition was elicited, but throbbing of the heart was complained of by some patients, and this also seems to indicate change in the muscular contraction independent of the inhibition. I allow that this evidence is very unsatisfactory compared with that given for the inhibitory action, but more adequate proofs can only be expected when more satisfactory methods of measuring the strength of the cardiac contraction are available. At present, we can measure only the rhythm.

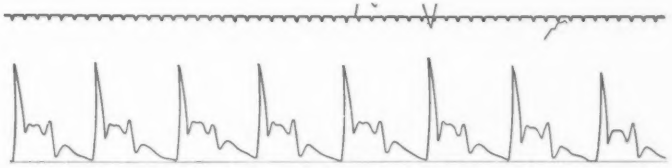

FIG. 4.—Tracing of radial pulse under digitalis, showing extrasystole after each normal pulse movement (continuous bigeminus).

Another feature which occurs in animal experiments is the increased excitability of the heart muscle, which makes itself apparent by a tendency to premature contractions or extrasystoles in the ventricle, or auricle and ventricle. These we have very often elicited in patients under full doses of digitalis in the form of more or less frequent extrasystoles (Fig. 4). This augmented irritability is unquestionably the result of the direct muscular action of the drug for, though its occurrence may be favored by slowing of the heart, it often arises in patients who do not present this feature in marked degree. Wenckebach states that extrasystoles may disappear under digitalis medication, but this form of irregularity is so capricious in its appearance that I am not disposed to regard digitalis itself as curative. Another feature which has repeatedly occurred in our cases, although more rarely, is pulsus alternans, in which the pulse beats and also the apex beats are alternately large and small without any difference in the interval between them. This form occurs especially after an extrasystole or after a pause of some duration (sinus slowing) and then gradually becomes less marked and disappears. It is met with in untreated cases of heart disease and is generally regarded as evidence of a serious reduction in the contractility. The most satisfactory explanation is that of Wenckebach, who regards the weak beat as the result of the prolonged activity of the preceding strong contraction. It may, in fact, be regarded as a condition in which the recovery of

energy by the heart is retarded, while the dissipation of energy during the contraction is not changed to the same extent or perhaps is unaltered. It may be suggested that digitalis by increasing the contraction power of the heart without a corresponding effect on the restorative function may occasionally tend to favor the development of this abnormality in hearts which are predisposed to it.

Turning to the second group of cases, those in which the node of Keith and Flack has lost its leadership, and the rhythm arises from some other part of the auricle, we find that digitalis has a much more striking effect. In fact it may be questioned whether it would have attained its position as *the* cardiac remedy had it not been for its efficacy in this condition, in which its exhibition is often followed by a truly wonderful improvement. The commonest form of this abnormal rhythm is that known as auricular fibrillation, and there is every reason to infer that a number of Withering's cases were of this description.

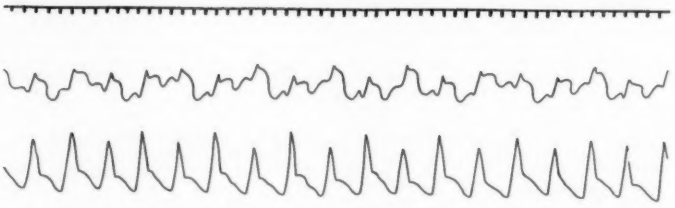

FIG. 5.—Tracing of radial pulse and apex (upper) under digitalis, showing alternation in artery and apex.

In this condition, which has long been known in animals, the auricle is distended and a continual tremulous movement occurs in its fibers, but there is no coördinated contraction, the fibers moving quite independently of each other. Irregular impulses are constantly discharged to the ventricle, which responds with a very rapid and quite irregular rhythm. In man, the condition was first defined by Mackenzie's observations on it, and is characterized by extreme irregularity of the pulse and by the absence of all signs of auricular activity. Its true pathology has only been determined recently. In our cases of this condition, the exhibition of digitalis was generally followed by rapid improvement. It is true that it did not restore the normal rhythm, but the symptoms of heart failure disappeared much more rapidly than in cases of the first group in which the normal rhythm was preserved. And coincidently with this improvement in the general symptoms the rate of the pulse fell from 120–150, to 60–70 or less.[5] The

[5] To ascertain the heart rate with even approximate accuracy in these cases, a record of the pulse must be taken or the heart sounds counted.

pulse remained irregular, but the irregularity was less marked (Fig. 6), and the beats were much stronger; the dyspnœa was relieved and the other symptoms of distress underwent marked improvement. The patient was often able to return to his work if it was not of an exhausting nature.

The most striking objective symptom was the fall in the pulse rate, which offered a marked contrast to that observed in the first group of cases. In these, in which the rhythm arose from the normal position, only about 30 per cent. of the cases reacted to digitalis with slowing, while 11 out of 12 of our cases of fibrillation, or 90 per cent., showed unmistakable slowing. In the twelfth there was fever present and no slowing occurred. The pathology of the condition suggests that this slowing is due to fewer impulses

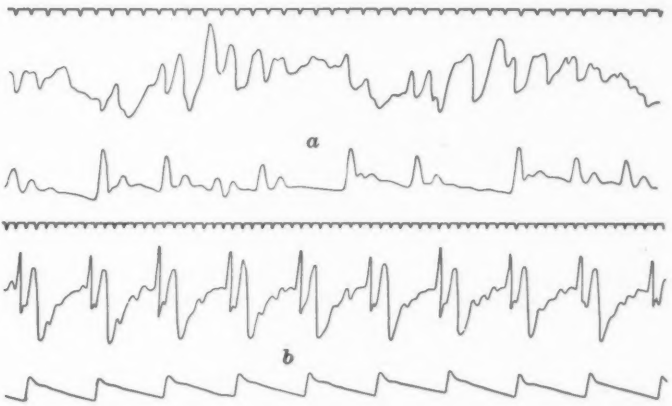

FIG. 6.—Tracing of the jugular (upper) and radial pulse (lower) in a case of fibrillation of the auricle (*a*) before treatment, (*b*) after treatment for some weeks with digitalis.

reaching the ventricle from the auricle. The condition of the last chamber is unchanged as far as our means of observation teach us, and there seems no other plausible explanation of the fall in the pulse rate than a diminution in the impulses passing the bundle of His. Moreover, in some rare forms of auricular delirium the pulse though completely irregular is not accelerated, and here there is reason to believe that the impulses from the auricle are partially blocked in their passage to the ventricle; in these cases digitalis does not slow the heart nor cause any marked improvement. Wenckebach has shown that stimulation of the inhibition by pressure on the vagus in the neck in auricular fibrillation induces the same slow pulse as occurs under digitalis, and in a case in which this procedure was ineffective, digitalis also failed to improve the rhythm. One is, therefore, tempted to

attribute the remarkable effects of digitalis in the ordinary forms of auricular fibrillation to its inducing a partial block of His' bundle[6] and thus relieving the ventricle from the continual bombardment with impulses from the auricle; that is, the digitalis action here would appear to be pure inhibition. And this explanation is supported by our experience in a number of cases in which the distress disappeared as the pulse fell, and when the treatment was given up for a few days the pulse accelerated, and almost step by step with the acceleration of the pulse, the dyspnœa returned.

In several cases the question has been further tested by the injection of atropine in sufficient quantities to put the inhibition out of action. For example, in a case of fibrillation in which the pulse was originally 150–170, but in which it had been reduced by digitalis to 60–70 per minute, $\frac{1}{50}$-grain atropine sulphate hypodermically accelerated the pulse to about 120. This seems to suggest that the inhibition was a large factor in the effect, though not the only one, for though the pulse was much accelerated by atropine it did not regain its original rate. In another case in which the original rhythm was about 150 per minute, it was reduced to about 50–60 by large doses of digitalis (15 minims four times a day). The patient left the hospital and continued to take digitalis as he felt the need of it, gradually reducing it until after some months he found that his pulse remained slow without the drug, and he only took about a drachm when it began to accelerate, about once a week. Yet on giving atropine at this time the pulse at once rose to 150 per minute, that is, to its original rate. In this case there seems no question that the conduction was reduced permanently by inhibition or, rather, that the inhibition had gained a permanent control over the heart, which was absent before the digitalis was given. Whether this is due to the prolonged inhibition to which the heart had been subjected by digitalis in the hospital, or whether the nutrition of the organ had been altered by some other effect of digitalis, *e. g.*, on the heart muscle, I am unable to say. And the fact that our methods give no sufficient indication of the changes in contraction power must render us careful in the interpretation of the symptoms. But I think I am safe in stating that we have no definite evidence that digitalis exerts any action apart from the inhibition in these cases of auricular fibrillation and that the proved fact of inhibition explains all the features observed.

When digitalis is pushed in auricular fibrillation it often reduces the rate still further to 40–50 per minute and induces "coupled beats;"

[6] Another possible interpretation may be suggested: In auricular fibrillation inhibition makes the tremor of the auricle finer in character, and perhaps the impulses transmitted to the bundle of His are weaker and thus fewer of them reach the ventricle. Digitalis may, therefore, slow the ventricle by weakening the impulses from the auricle rather than by increasing the difficulties in their passage.

that is, each beat of the ventricle is followed at a very short interval by a second weak contraction and then by a long pause (Fig. 7). The electrocardiograph indicates that the first strong contraction originates in the normal way by an impulse reaching the ventricle from the bundle of His, while the second weak one is a true ventricular extrasystole. In one of our cases in which "coupled beats" were present, atropine accelerated the rhythm of the ventricle by improving the conduction in the bundle and as the rate increased the coupled beats became fewer and finally disappeared. This suggests that the irregularity was at any rate, in part the indirect result of the slow rhythm which allowed the irritability of the ventricle time to develop, and that here the extrasystole resulted indirectly from the inhibition.

FIG. 7.—Tracing of apex beat (upper) and radial pulse (lower) in fibrillation treated with large dose of digitalis. In the apex tracing an extrasystole is seen to follow each normal beat (coupled beats or continuous bigeminus). These are too weak to cause a pulse in the radial.

In animals I have often observed auricular fibrillation occur from very large quantities of digitalis from excessive stimulation of the auricle muscle. It is of interest to note that in two cases we have met with the same phenomenon in patients. In one of these digitalis had been given for some time without slowing the pulse which maintained a rapid regular rhythm. Suddenly the rate fell to about 70 and the heart became quite irregular. All evidence of auricular activity disappeared—no *a* wave in the jugular pulse, disappearance of a presystolic murmur which was formerly present—in fact a typical picture of auricular fibrillation under digitalis was presented. With equal suddenness the fibrillation disappeared and the former rapid normal rhythm was restored, when the drug was abandoned.

Here it might be supposed is certainly an instance where the muscular action was the cause of the irregularity, for the irritability of the heart muscle is augmented by the direct action and culminates in fibrillation. I would not deny the explanation, but I may remind you that fibrillation may occur from inhibition, so that it is possible that here also the action is central.

Apart from auricular fibrillation we have met two cases in which

the rhythm was given by the auricle, but which it was quite regular though extremely rapid. In these digitalis reduced the rhythm quickly and brought relief from the dyspnœa and other symptoms. In one of them the slowing was interrupted by short phases of what seemed auricular fibrillation, but these became less frequent as the heart rate fell to the normal. The slowing of the pulse in these cases was comparable to that observed in cases of auricular fibrillation, and the question arises whether it was brought about in the same way by a diminished conduction of impulses from the auricle to the ventricle, or whether the actual discharge from the abnormal point in the auricle disappeared under the inhibitory action of the drug.

In any case the efficacy of digitalis and its allies in disorders of the heart arising from auricular hyperactivity is very striking, and raises the question whether the chief usefulness of the drug does not consist in its protection of the ventricle from the too exigent demands made on it by the auricle.

I have given you some instances in which the inhibitory factor seems to play an important, perhaps a dominant part, in the effects of digitalis in therapeutics. Let me remind you of one in which the muscular action alone is desirable. In partial or complete block the indications are to accelerate the ventricle and relieve the symptoms of arrest of the circulation which culminate in the Stokes-Adams syndrome. Bachmann, I think, was the first to utilize the muscular action of digitalis for this purpose, but it might be preferable to employ a member of the series without its inhibitory action, and in future cases I would suggest the use of helleborein or of a mixture of helleborein and digitalis.

The question as to the respective roles played by the inhibitory and the muscular factor in digitalis is not of theoretical interest only. For if the therapeutic effects are due to inhibition only, they might be elicited by other drugs which do not possess the unpleasant effects on the alimentary tract which present themselves under digitalis. On the other hand, if the muscular action is the essential factor, it might be possible to discover a drug possessing this without the inhibitory effects. In any case it seems desirable that we should be able to vary the proportions of these two factors, for there is no reason to suppose that digitalis presents the exact combination which is suitable in all cases. We, therefore, have treated a number of cases of heart disease with aconite and aconitine, which is reputed to slow the human heart by stimulation of the vagus centre, but has not the digitalis action on the cardiac muscle. But Dr. Price, who has carried out this investigation, finds that aconite does not deserve its reputation in this respect, for it failed to slow the heart even when pushed until unpleasant symptoms appeared; yet these cases afterward responded to digitalis by slowing. On the other hand, we have tried helleborein

which possesses the muscular effect of digitalis without its action on the inhibition, but the results were not satisfactory for although no slowing occurred no definite improvement followed in our cases. This may be partly owing to the fact that helleborein tends to cause diarrhœa when given in adequate doses, and we intend to continue its investigation further.

These experiences have led us to make a systematic comparison of the members of the digitalis series in therapeutics. As yet we have taken up chiefly the three common members, digitalis, strophanthus, and squills, and these we have used in the form of the tinctures, as this seemed to be of more importance than the pure principles, which are comparatively seldom employed. Our method is to give digitalis tincture first and push it until it fails to induce further improvement and unpleasant symptoms arise; then all medication is suspended for ten days or more and the patient very often relapses to his former state. Tincture of strophanthus is then given in the same way, again an interval is allowed and finally squills is prescribed; the order is not always the same of course. We have made some interesting observations for the details of which I must refer to a paper by Turnbull which will appear soon from Mackenzie's clinic. Among these I may mention that we find the tincture of digitalis (B. P.) to be nearly twice as powerful as that of squills or strophanthus, although they have been used in the same dose for many years.[7] Both the therapeutic effects and the untoward symptoms of squills or strophanthus are only elicited when they are given in nearly twice the dose of digitalis.

In reading Withering's account of his treatment one is struck by the fact that he always induced vomiting as soon as possible and then continued his treatment with smaller doses. We have not gone so far as the pioneer, but we have found again and again that the best results are obtained only by the largest doses which can be given without gastric and intestinal symptoms. The dose which we find advisable is a dram to a dram and one-half per day of digitalis tincture, or a dram and one-half to two drams of tincture of squills or strophanthus (B. P.). This, of course, is twice as much or more than is ordinarily prescribed, and I must confess that not infrequently there arises nausea and occasionally vomiting, or sometimes severe headache from the higher dose. But on the other hand, we have patients taking a dram of digitalis per day for months and sometimes going to work under this regime.

[7] These relations hold only for the tinctures of the B. P. The tincture of strophanthus (U. S. P.) is four times as strong as that of the B. P., and according to our results the efficient dose of this would be about one-half that of the tinctura digitalis (U. S. P.) and this is the proportionate dose actually suggested in the U. S. P. The tincture of squills (U. S. P.) on the other hand, is only one-half the strength of that of the B. P., and our results would suggest it being given in three or four times the dose of tinct. digitalis U. S. P.

There is no question that digitalis and its allies are too much feared by the medical profession. The "cumulative" action has been held over us as a bogey for so many years that many prescriptions contain this valuable drug in harmless and useless doses. *Non nocere* is a good rule, but *prodesse* is a better, and tincture of digitalis in two minim doses three times a day approaches the line of purely expectant treatment.

As regards their relative usefulness there is little difference between these three drugs. We get the same beneficial results and the same undesirable ones as regards the heart, and a patient who shows symptoms of heart block under digitalis, suffers from the same irregularity under squills or strophanthus, while when extrasystole is induced by one it follows from all. Strophanthus is often said to have less tendency to raise the blood pressure than digitalis, but in our patients neither induces any rise of pressure and in some both cause an equal fall. There is, on the whole, rather less tendency to headaches, nausea, and vomiting under strophanthus and squills than under digitalis, but the difference is not very marked and headache is caused in some cases by all three. Slight diarrhœa has followed the use of squills more than the others, and strophanthus also tends to cause this more than digitalis. This tendency to diarrhœa is still more marked from the use of helleborein and apocynum which we have begun to work upon.

In animal experiments, one of the characteristic effects of digitalis medication is the rise of blood pressure, which arises in part from the heart action, in part from a constriction of the arterioles. In patients the blood pressure is rarely augmented by digitalis and may in fact fall, as the general improvement sets in. This is, I think, due to the much greater efficiency of the vasomotor mechanism in man, which has been developed to permit of his assuming the erect attitude. As the heart fails in disease, the organ which first suffers is the brain; but anemia of the brain is promptly remedied by constriction of the abdominal vessels, by which the blood is again directed to the head areas. If, now, digitalis is given and the heart action improves, the first effect would be to increase the blood supply of the brain, and this leads the sentinel in the medulla to relax its vigilance, the mesenteric vessels are allowed to relax and the improvement in the heart may thus be coincident with lowered blood pressure. In our experience there is no significant increase in the urine except when dropsy is present.

In the course of this investigation I have been struck by the small amount of accurate knowledge that we possess as to practical therapeutics. My experience has been almost exclusively in the laboratory and perhaps I have expected too high a standard in the clinic, but in this field of cardiac tonics alone I see an endless vista of questions to be solved in the clinic if only accurate observations

are available. There seems to me to be no field in which painstaking work is more required and in which the prospects of success are more promising than in clinical therapeutics. I would commend the cultivation of this study to any one who wishes to add to the general store of medical knowledge and at the same time to devote himself to some line of work which will bear upon his own future work. But we have enough of inaccurate therapeutics already; what is needed is not a statistical compilation, but an accurate study of each individual case and a careful and, if you will, an experimental investigation of each feature presented.

PERSONAL EXPERIENCES WITH THE USE OF SALVARSAN (DIOXYDIAMIDOARSENOBENZOL, OR "606") IN THE TREATMENT OF SYPHILIS.[1]

By Hermann Goldenberg, M.D.,
ATTENDING DERMATOLOGIST TO THE MOUNT SINAI HOSPITAL,
AND
David J. Kaliski, M.D.,
ASSISTANT IN SERUM RESEARCH, MOUNT SINAI HOSPITAL, AND ASSISTANT IN GENITO-URINARY DISEASES IN THE MOUNT SINAI HOSPITAL DISPENSARY, NEW YORK.

Case XVIII.—S. M. K., aged twenty-three years, acquired lues three years ago. Following the appearance of the secondary roseola, the patient was given a course of injections of salicylate of mercury. The injections were badly borne, causing symptoms of mercurial poisoning. From time to time mucous patches appeared in the mouth, and headache was an almost constant symptom. After a freedom from medication for more than six months, the patient was given one injection of bichloride of mercury (2 per cent., 10 minims), which was followed by bloody diarrhœa, nausea, vomiting, and salivation lasting for about a week. No further attempt at mercurial medication was made. In October, 1910, the Wassermann test was positive. In November, 1910, the patient developed mucous patches on the tonsils. The Wassermann reaction was positive. On November 15 the patient received 0.5 gram of an alkaline solution of "606" into the right buttock. The injection caused pain throughout the night following the giving of the drug, which was readily controlled by morphine. The patient was out of bed the next day, and the further course of the case was uneventful. The mucous patches on the tonsil disappeared within twenty-four hours. The patient on January 15 was free from all signs of lues. The Wasserman reaction was negative. On February 1, 1911, the reac-

[1] Concluded from page 429.

tion was again positive, although the patient is still free from all signs of lues.

CASE XIX.—P. B., aged forty-five years, had an initial lesion four months before admission. He came to the hospital with a profuse miliary syphilide over the entire trunk and extremities. He had an enormous enlargement of all the glands of the body, especially of the occipital, mastoid, preauricular and parotid, cervical, submental, submaxillary, axillary, etc. The Wassermann test was positive. On December 18, 0.6 gram of an alkaline solution of "606" was injected into the left gluteus. On December 25 the eruption on the chest and upper part of the back had, to a great extent, disappeared, and on the abdomen and back the lesions had coalesced and were desquamating. The lymph nodes were unchanged. On December 31, the day of his discharge, most of the eruption had disappeared, leaving brownish pigmented spots. On the abdomen and extremities there was still a diffuse scaliness, but no definite luetic lesions could be made out. The glands were about half their original size, but still very large. The temperature rose on the day following the injection to 101.5°, but then came down to normal. The Wassermann test was positive. On January 12 the eruption had entirely disappeared, but a general brownish pigmentation was still visible. The lymph nodes were somewhat smaller than on the previous examination, but still remained very large. The Wassermann test was positive.

CASE XX.—S. R., a housewife, aged twenty-two years, entered the hospital on December 20 after having been confined to bed for four weeks with fever, excruciating pains in the tibiæ and arms, which prevented her from sleeping at night, and a pustular crustaceous syphillide on the face and back, mucous patches on both tonsils, and extreme tenderness over the bones of the forearms, wrists, and tibiæ. The temperature ranged between 99° and 102°. The Wassermann test was positive. On December 22 she received 0.6 gram of an alkaline solution of "606" into the right gluteal muscle, which caused very little pain. On the night following the injection the pain over the tibiæ was more severe than ever. The next day, less than twenty-four hours after the injection, the pain had left her entirely and did not reappear. There remained, however, tenderness on pressure over both tibiæ for over a week. The mucous patches healed within six days. All the skin lesions disapprared within ten days, leaving pigmented spots, with the exception of two papules on the neck and forehead, which were still present on January 12. The Wassermann test on January 7 was positive.

CASE XXI.—H. M., aged twenty-three years, was admitted to the hospital on January 3, 1911, with a maculopapular syphilide, general adenopathy, and mucous patches on the tonsils and tongue; and in the middle of the latter there was a deep ulceration with a dirty base, measuring 1.5 by 1 cm. in size. The two initial lesions,

which had appeared on the penis, were present as scars. The Wassermann test was positive. Spirochetes were found in the mouth lesions. On January 3 he received 0.2 gram of "606" in liquid paraffin in the left buttock muscles. On January 4, 0.1 gram of the drug was injected in paraffin. On January 5 the patient stated that the pain in the ulcer of the tongue on swallowing had disappeared, but there was no visible change in the lesion. On January 6, 0.25 gram of the drug was injected in a similar manner. On January 8 the mucous patches on the tonsils had entirely healed and the eruption was fading. The ulcer on the tongue was clean and was healing. On January 9 he received 0.25 gram of "606" in paraffin oil as before. On January 10 the eruption had disappeared, the ulcer on the tongue was present, but was epithelializing. On January 14 the ulcer on the tongue had entirely healed and the patient was free of all manifest symptoms. The injections were almost painless, but were followed by a rise of temperature to 101° on the day after the injections. The last two injections of the drug, rubbed up in paraffin, left a marked induration, which was tender to touch. The Wassermann test on January 14 and January 21 was positive.

Case XXII.—M. S., aged twenty-four years, contracted a chancre six months ago, for which he received thirteen injections of bichloride of mercury and two of the salicylate. He was referred to the hospital on November 15, 1910, with mucous patches on the tongue. It was thought that the lesions would yield readily to active mercurial treatment by injection, and the patient was referred to the dispensary, where he was given six salicylate of mercury injections, without any improvement. He was readmitted to the hospital on January 1 with mucous patches on the lower lip and tonsils and a hypertrophic erosion on the side of the tongue. There was also a small papule on the upper aspect of the scrotum. The Wassermann reaction was positive. On January 3, 1911, he received 0.2 gram of "606" by injection into the buttock. The drug was rubbed up with liquid paraffin. On January 4 he received 0.15 gram in paraffin in the gluteus of the opposite side. On January 6 he received 0.25 gram into the buttock. On January 8 the mucous patches on the lips and tonsils had healed and the hypertrophic papule on the side of the tongue was flat and on a level with the surface of the tongue. Epithelialization had begun. January 9 he received a fourth injection of 0.25 gram in liquid paraffin into the buttock. On January 11 all the mucous patches had healed, the papule on the side of the tongue leaving a grayish discoloration. This had disappeared by the 14th. The Wassermann reaction on January 14 was positive. Following each injection of the drug there was a rise of temperature to 101°, which quickly came down to normal. The injections were practically painless, so that it was not necessary for the patient to remain in bed.

CASE XXXI.—Mrs. M., aged forty-one years, acquired lues in September, 1908. Since that time she has had very vigorous treatment with inunctions and injections. When seen on December 10 she had relapsing mucous patches on the tip of the tongue, a circinate syphilide on the left arm, and severe headache. On December 12, 0.5 gram of an alkaline solution of "606" was injected into the left gluteus. She left the hospital on the following day, having had but slight pain. When seen again on January 6 all the lesions had disappeared, a brownish pigmentation being left at the site of the syphilide. The headaches have entirely disappeared.

CASE XLVIII.—A. K., aged forty-five years, entered the hospital in November, 1910, with a maculopapular syphilide and mucous patches. There was no history of initial infection obtainable. She was discharged after a course of injections of mercury without lesions. The Wassermann reaction was positive. In the beginning of January, 1911, she developed vertigo and dimness of vision, and upon readmission to the hospital on January 5 both vitreous chambers were diffusely cloudy, so that the disks could not be seen. Vision in the right eye was $\frac{10}{200}$, and in the left eye $\frac{6}{200}$. The diagnosis of specific chorioretinitis having been made by Dr. May, the attending ophthalmologist, the patient, on January 9, received 0.6 gram of an alkaline solution of salvarsan. The pain and vertigo disappeared within five days and the cloudiness of the vitreous chambers cleared up in a week, so that the fundi could be seen. Both fundi were found very much blurred. On January 24 the vision had improved, the right eye being $\frac{20}{30}$, the left eye, by the aid of a spherical lens—0.75 lens, $\frac{20}{70}$. The disks were still blurred. The patient had gained in weight and her general condition was improved. The Wassermann reaction was positive.

IV. *Tertiary Lesions and Gummas.*

CASE XXIII.—M. L., aged thirty-one years, and married, with healthy children, had an initial lesion six years ago. One year ago he noticed an enlargement of both testes, for which he received several series of deep injections of salicylate of mercury, with slight amelioration of the condition. The testes and epididymes on both sides were hard, nodular, and uniformly enlarged, so that the testes and epididymes could not be separated. The Wassermann test was positive. On October 16, 1910, the patient received 0.6 gram of "606" in neutral emulsion, which caused considerable pain, requiring control by morphine. On October 20 both testes were much softer and lighter in weight. On November 13 the testes and epididymes could be made out separately. The gummatous infiltration was much smaller and softer. The Wassermann test was positive. On December 4 the size of the testes on both sides was normal, but there

was left a distinct thickening of the lobus major and minor of both epididymes. The Wassermann test was positive. On January 22, 1911, the left testicle was absolutely normal. The right testicle showed a very small nodule in the upper part of the epididymes. The patient had no pain, had gained in weight, and feels better than he did in the last ten years.

Case XXV.—S. F., aged thirty-one years, acquired an initial lesion on the penis four years ago. He came under our notice three years ago with a destructive gummatous process of the glans penis, which had resisted prolonged treatment with mercury injections. Under treatment with salicylate of mercury injections, using large doses, the gummatous ulceration of the glans penis healed, but he developed multiple gummas of the muscles of various parts of the body. Every one of these broke down while the patient was treated with salicylate of mercury injections, of which he received over seventy. About seven months ago he noticed a swelling of the left knee, with pain and difficulty on walking. This persisted in spite of the above-named treatment. At the time of his admission to the hospital he had a broken-down gumma on the buttocks, an unbroken deep gumma about the size of a horse-chestnut over the left sternoclavicular junction, and a syphilitic synovitis of the left knee-joint, with effusion obliterating the normal outlines of the joint. Wassermann reaction was positive. On October 4, 1910, he received 0.6 gram of a neutral emulsion of "606." Four hours later his temperature reached 102°, dropped then to 99°, and rose on October 8 to 102.8°; on October 11 to 104°. Simultaneously a sharply circumscribed, slightly elevated red area, 6 by 8 inches, was observed surrounding the site of the injection. A beginning erysipelas was suspected and the patient isolated. Coincidentally with the rise of temperature there occurred a diminution of the gumma at the sternoclavicular junction, and an improvement in the broken-down gumma on the buttock. The ulcer became shallower and the base cleaner. On October 12 the swelling and redness had disappeared and the diagnosis of erysipelas was abandoned. A blood examination at this time showed 8000 white blood cells and a normal differential count. The evening of this day the temperature rose to 105.4° and was accompanied by several severe chills and a follicular tonsillitis. Simultaneously with this rise in temperature there occurred marked diminution in the size of the affected knee. It was also noted that over a number of old gummas which had already cicatrized there were formed crusts, the margins became red, and on the glans penis, which was deformed by numerous scars, a serous liquid exuded from three sinuses. This modified Herxheimer reaction lasted twenty-four hours. On October 24, the day of his discharge from the hospital, the left knee-joint was normal, the ulcer on the back had healed, and the fistulous openings on the glans penis, which had been present for three years, had entirely closed. The

patient did not present himself for examination until December 15, at which time he was found to be absolutely well, had gained twelve pounds in weight, and was in perfect condition, with the function of the knee perfectly restored. On January 25, 1911, the Wassermann test was positive; his general condition was as on December 15.

CASE XXXII.—R. B., aged twenty-four years, had an initial lesion two years ago. He presented himself with cutaneous gummas over the left eyebrow, above the left ear, above the left scapula, on the right side of the lumbar spine, and on the right thigh, of about four months' duration. During the last three months he has been unable to work on account of weakness, and has lost considerably in weight. The Wassermann reaction was positive. On October 26, 0.6 gram of a neutral emulsion of "606" was injected under both scapulæ. There was considerable pain after the injection, which disappeared the next day. About one week after the injection of the drug the eruption had entirely disappeared. The Wassermann reaction was very faintly positive. There was great improvement in the general condition of the patient; he gained ten pounds in weight in two weeks.

CASE XXXIII.—I. S., aged sixty-three years, had a small lesion on the penis forty-four years ago, for which he received only local treatment. No other lesions were noticed up to the time of onset of his present trouble. For the last three months he has noticed a hard swelling on the left side of the tongue, which gives him a great deal of pain on eating and difficulty in swallowing. There was on the left border of the tongue a tumor about the size of a plum-pit, which was ulcerated on the surface. The right and left submaxillary nodes were enlarged. The Wassermann reaction was positive. On October 26, 0.5 gram of a neutral emulsion of "606" was injected in both infrascapular regions. The injection caused some pain, which was controlled by morphine. The lesion on the tongue did not show any change during the patient's five-days' stay in the hospital, nor during subsequent observation at the dispensary for four weeks. Biopsy was then made, showing the tumor to be an epithelioma, probably arising on the base of an old luetic scar.

CASE XXXIV.—G. R., aged thirty-three years, married, has four healthy children and never had any abortions. Two years ago she noticed an ulcer on the left knee, which healed in the course of a year, only to break open again. For the last year the ulcer has been gradually growing larger. Now she cannot walk on account of the lesion on the knee. Examination showed a large, irregular, serpiginous ulcer about the size of a large palm of a hand on the anterior and inner aspect of the left knee, the edges and base of which were covered with exuberant granulations, showing little tendency to epithelialize. The eye-grounds were negative. The urine was negative; the leukocytes, 8800; and the differential count normal. The Wassermann reaction was weakly positive. On October 15, 0.6

gram of "606" was injected in the subcutaneous tissue under the left scapula according to the method of Wechselmann (neutral emulsion). Soon after the injection, and for many days thereafter, there was about the site of the injection a gradually increasing redness and some infiltration. The latter increased in size until in about a week it had assumed the size of a large lemon. There was marked tenderness, redness of the surface of the mass, and some fluctuation. Within two weeks after the injection the mass showed distinct fluctuation, broke down, and a slough of the tissues began to separate. In the course of the next month the slough gradually diminished in size, but had not completely separated under conservative measures until about two months more elapsed from the time of the injection of the drug. After the drug was injected the wound showed from the very first day evidence of healing. The progress was most marked for the first ten days, in which time more than half of the large ulcer had epithelialized. The healing was more sluggish subsequently, but within five weeks after the patient received the drug the ulcer had entirely healed. One week after the injection the Wassermann reaction was negative. The general condition of the patient improved and she gained weight. Up to the time of writing there has been no return of the ulcer. The Wassermann reaction was positive nine weeks after the injection

CASE XXXV.—M. G., aged thirty years. No history of lues was obtainable. The patient was referred to the hospital by Dr. Abraham Jacobi with a large perforation involving the bony and cartilaginous portions of the nasal septum. The soft palate was destroyed on the right side, the uvula markedly hypertrophied and infiltrated, preventing a view of the posterior nares. The pharynx was hyperemic, with two ulcers covered with dirty gray slough. There was necrosis and hypertrophy of the epiglottis; the upper one-half was totally destroyed, the stump irregular, nodular, and thickened; and the false vocal cords were hypertrophied. There was a small ulcer on the inner side of the right calf which, on account of its appearance and its concomitance with varicose veins, was considered a varicose ulcer. The patient was hoarse and had severe pain on swallowing. The Wassermann reaction was positive. On November 7, 0.5 gram of an alkaline solution of "606" was injected into the left gluteal region. It was followed by severe pain, which lasted for twelve hours. Twenty-four hours after the injection the patient was able to eat solid food and could swallow without pain. On November 11 the pharyngeal ulcers were cleaner and smaller, and the uvula was much less infiltrated and freely movable. The temperature since the injection varied between 100.4° and 102.4°. On November 14 the pharynx was almost entirely cured, but the uvula was still thickened, though freely movable. The epiglottis showed no more induration, but still a slight grayish appearance of the stump. The patient was discharged cured on November 17.

On December 1 examination showed a normal condition of the pharynx and larynx. The small varicose ulcer, which had markedly improved while the patient was in bed, was in about the same condition as before the injection was made, confirming our original view that it was not a gumma.

CASE XXXVI.—M. V., aged thirty-nine years, has syphilis of twelve years' standing. For the past six weeks he has a painful ulcer of the soft palate. To the right of the base of the uvula there was a punched-out ulcerated area, about one-eighth of an inch deep and half an inch in diameter, covered by a dirty slough. The Wassermann test was positive. On December 7 he received 0.6 gram of an alkaline solution of "606" into the left ileocostal muscle. There was very little pain, and the patient left the hospital on December 11 with no appreciable change in the condition of the gumma. The pain, however, had entirely subsided. On December 17 the ulcer was clean and healing, with only a superficial erosion left. On December 24 the ulcer had entirely healed. The Wassermann test was positive.

CASE XXXVII.—Mrs. R., aged thirty years, contracted a very obstinate lesion on the lip about ten years ago, and has had three miscarriages and one viable fœtus, with symptoms of syphilis. She has undergone repeated and strenuous antispecific treatment with injections. She has now two seemingly healthy children. Since the birth of the last child, eleven months ago, she has complained from time to time of pain over the region of the liver and occasional attacks of fever. On October 19 she took to bed, and Dr. A. A. Berg, being consulted, advised an exploratory laparotomy. The liver border was found sharp and not nodular and no nodules were detected on the anterior surface of the liver, but multiple gummas were detected on the under surface. The diagnosis of gumma was confirmed by the pathologist, Dr. F. S. Mandlebaum. The pain from which the patient suffered persisted after the operation. Twenty days later the patient received 0.6 gram of an alkaline solution of "606" into the gluteal muscle. The patient left the hospital one week after the injection. Her attending physician, Dr. Morris Stark, has informed us that soon afterward the pain over the liver region disappeared entirely, and up to the time of writing she has remained free from pain. The patient states that she feels better now than ever before in her married life.

CASE XLIII.—M. P., aged twenty-eight years, was referred by Dr. Emil Mayer with the following history: A chancre was acquired eleven years ago; he was treated for one year. In November, 1910, it was found that he had a perforation of the cartilaginous septum about the size of a quarter, and of the soft palate, a painful induration over the right nasal bone, and complete obstruction of the right side of the nose, which was filled by large crusts. Upon removal of the latter a mass was seen springing from the upper portion of

the inferior turbinate, and a probe introduced into the nasal bone, showed erosion of the bone. A diagnosis of gumma of the right side of the nose, with beginning ulceration and destruction of the nasal bone, was made. A portion of this gumma was removed, and it was then seen that there was also an ulceration within the right ala. The Wassermann reaction was positive. On November 14 the patient received 0.6 gram of an alkaline solution of "606" into the gluteal muscle, causing very slight inconvenience. He left the hospital within twenty-four hours. On November 16 the tenderness over the nasal bone had disappeared. On November 28 it was found that the ulcer on the ala was entirely healed and that there was very little crust formation, no roughened edges of bone, and no sign of the gumma. The bulging appearance over the right nasal bone had disappeared and breathing was free and unobstructed. On January 4, 1911, there was no crust formation, the nasal bone was no longer painful or tumefied, and the right side of the nose was the better of the two. The Wassermann test was positive. The patient relapsed on January 11 with a destructive gumma of the septum. He lost twenty pounds in weight. He is now under treatment with mercurial injections.

Case XLVII.—G. S., aged thirty-five years, contracted an initial lesion twelve years ago. For the last five years he has been troubled with recurring squamocircinate syphilides upon the face and trunk, for which he underwent treatment at Hot Springs (five courses of inunctions in as many years). In August, 1910, he had sixteen enesol injections. He entered the hospital on January 9, 1911, with multiple patches of a squamocircinate syphilide upon the face and trunk varying in size from a dime to a silver dollar. The Wassermann reaction was negative. On January 9 he received 0.7 gram of an alkaline solution of salvarsan. This caused severe pain, lasting a week. Ten days after the drug was given all the lesions had disappeared. The Wassermann reaction a few days after the injection was negative. This result exceeds in completeness and rapidity of action anything which we have observed after the injection of salvarsan. As to the permanence of the cure, the time elapsed since the injection is too short to permit of an opinion at this writing.

V. *Latent Syphilis.*

Case XXIV.—F. P., aged forty-five years, acquired lues about nine years ago. For about one year following the development of secondary lesions he received treatment with protiodide of mercury in pill form and iodide of potassium. For more than seven years following this treatment the patient received no further medication, and so far as he knows there were no further lesions. About a year ago, desiring to marry, he returned to his physician for examination,

to learn whether he was free of specific taint. Physical examination was negative, but the Wassermann reaction, undertaken at this time, was positive. His physician then put him through a vigorous course of injections of bichloride and salicylate of mercury. Three Wassermann tests, taken at regular intervals, up to the time of his admission to the hospital, were successively less strongly positive, but there was still sufficient inhibition of hemolysis at the last test to call it positive. At the solicitation of the patient he was given an injection of 0.6 gram of an alkaline solution of "606" on December 24. The injection was given intramuscularly in the right buttock. It was followed by moderate pain and some stiffness, lasting about three days. Otherwise the injection was uneventful. On February 5 the patient was still free from any manifestations of lues. The Wassermann reaction was weakly positive.

VI. *Hereditary Syphilis.*

Case XLI.—P. R., aged five years, acquired syphilis at the age of seven months from a wet nurse who was found to be syphilitic. The general eruption at that time disappeared under mercurial inunctions. Three years ago the child developed lumps on the legs and abdomen, which broke down, discharging a serous fluid. Since then he has had repeated attacks of similar lesions on various parts of the body. One year ago he began to get hoarse and became very dyspnœic from laryngeal obstruction; this yielded to mixed treatment, but recurred six months ago and required tracheotomy. Two months ago a swelling of the left index finger and of the bone below the right elbow was noticed. The Wassermann reaction was positive. The mother gave a negative reaction. On December 23, 0.15 gram of an alkaline solution of "606" was injected into the left gluteus. On the following day an erythematous rash appeared on the body, lasting a few hours. On December 28 the swelling of the finger was much improved and the thickening of the elbow less, the measurement showing a diminution of 0.75 cm. There was considerable pain at the site of the injection, disabling the child. The temperature rose on the second day to 101.5°, and remained at 100° for two days. On January 21 the patient was able to walk without difficulty. The periostitis of the finger was almost entirely gone. The swelling of the elbow was only moderately improved.

Case XLII.—B. S., aged fourteen years, entered Mt. Sinai Hospital on February 16, 1910, on account of swelling and tenderness over the right leg. The mother had four children and three miscarriages at three to four months; one brother has hereditary lues and has a similar swelling about his left ankle. The patient was treated with mercurial inunctions until March, 1910, without benefit. She then developed a mild mercurial nephritis, and was then treated

with Zittmann's decoction. She left the hospital unimproved on April 6, and was subsequently treated at Mt. Sinai Dispensary by injections of mercury. No improvement took place, and she was readmitted on December 26. The anterior edge of the right tibia was broadened and presented irregularities and nodosities, the thickening continuing down to the ankle. There was marked bone tenderness. The ankle was swollen, especially on the outer side, where the normal outlines are obliterated. The skin was discolored. Pressure over the malleolus caused much pain. The diagnosis was made of periostitis and osteo-arthritis. The radiogram showed considerable absorption of the lower end of the right tibia. The Wassermann reaction, which had been negative on the first admission, became positive on January 8, 1911, after injections of mercury. On January 10 she received 0.3 gram of an alkaline solution of "606" into the gluteal muscle, followed by moderately severe pain. On January 20 she received a second injection of 0.25 gram in liquid paraffin. Following the injection the pain subsided entirely. The swelling about the malleolus has practically disappeared. The tenderness over the tibia has disappeared, although the nodules are still present.

VII. *Cerebrospinal Syphilis.*

Case XXXVIII.—M. D., aged thirty-eight years, contracted lues eleven years ago. In May, 1910, he developed numbness and heaviness in both legs, carpet sensation under both feet, and incontinence of urine at times. The pupils reacted to light and accommodation. The knee-jerks and Achilles reflexes were absent; Romberg sign was present. He had slight ataxia of both lower extremities. He received by his attending physician, Dr. M. Radin, to whom we are indebted for these notes, thirty injections of bichloride of mercury. On September 20 there was a full ataxia of the lower extremities. On October 17 the Argyll-Robertson pupil appeared. On November 4, the Wassermann test being positive, he received 0.4 gram of an alkaline solution of "606" into the left gluteus muscle. There was slight temperature reaction, not over 101°, for the next three days. The patient was able to go about his business on the second day after the injection. On November 16 the pupils were found to react to light slightly. The subjective symptoms above enumerated improved. On November 22 a second injection of 0.45 gram of an alkaline solution of "606" was given, and caused very little pain. The patient was not confined to bed and there was no temperature rise. On December 5 the reaction of the pupils to light was more active. The reflexes were unchanged, likewise the ataxia. On December 23 the third injection of 0.45 gram of an alkaline solution of "606" was given, with no after-effects. On January 12 the knee-jerks were still absent, Romberg's sign was

present, the gait was ataxic but improved, the reactions of the pupils to light was present; the left reacted better than the right. There was great subjective improvement.

CASE XXXIX.—F. S., aged forty-one years, acquired lues twenty years ago. He had active treatment for several years. In February, 1905, diplopia, associated with frontal headaches and pain over the right parietal bone, developed. He had several attacks of diplopia, which always disappeared after active mercurial treatment. For the last eighteen months he has had almost complete freedom from ocular symptoms, but suffers from pain in the head. The patellar reflexes are always exaggerated. In the summer of 1909 he developed glycosuria and acidosis, which disappeared within a month, to reappear from time to time. In October, 1909, the Wassermann reaction was negative, but it became positive in October, 1910. On November 25 he received 0.45 gram of an alkaline solution of "606" into the buttock. Dr. F. S. Mandlebaum, who referred the patient to us for injection, has kindly informed us that the pain in the head is still present, though slightly less intense.

CASE XL.—A. S., aged thirty-six years, was seen by one of us (G.) in consultation with his family physician in 1909 and 1910. In spite of very energetic treatment with mercurial injections, he had a perforation of the hard palate. In the spring of 1910 he was confined to bed a physical wreck, unable to sit up, and seemed to be on the point of death. He was suffering from symptoms of cerebral lues. Under sixteen enesol injections, great improvement took place. There remained, however, a chain of nervous symptoms, namely, crying spells, lack of confidence to walk alone, pain in the right side of the head, dizziness, and, above all, diabetes insipidus with insatiable thirst. The patient had to drink between thirty and forty glasses of water a day, and never ventured out for even a short walk without a thermos bottle containing water. On November 21, after consultation with Dr. B. Sachs, who concurred in the diagnosis of cerebral lues, the patient was given 0.45 gram of an alkaline solution of "606" into the left gluteal muscle. The improvement in his mental condition was very slow, but the intense thirst soon subsided. The headache disappeared, but he still feels dizzy at night. The patient is now satisfied with five or six glasses of water a day. He has gained seven pounds in weight. He is able to go out accompanied, and is much more cheerful than before the injection. The inequality of the pupils has not changed, nor has the Argyll-Robertson symptom disappeared. On January 11, 1911, he received 0.3 gram of "606" in paraffin emulsion.

CASE XLIV.—S. F., salesman, aged forty-six years; does not remember primary luetic infection. Five years ago he developed an intranasal lesion, which was diagnosticated as a gumma. This yielded readily to antispecific treatment, but recurred two years later for a short time. For the last few years he has had attacks

of hemiplegia or numbness of the left side, associated with loss of consciousness, and involuntary urination and defecation, lasting one to seven days, and gradually subsiding. In the interval between these attacks his memory, previously good, frequently lapses. Two years ago he had an attack of arthritic pain, which yielded to antispecific treatment. He has received from his physician a very large number of mercurial injections and much potassium iodide. The patient responded intelligently to questions. His pupils were slightly unequal in size, but reacted normally to light and accommodation. His eye-grounds were practically negative. His reflexes were much exaggerated and his gait showed a slight weakness of the left leg, but no ataxia. The physical examination otherwise was negative. He is rather dull and stolid mentally. The Wassermann test was negative. On December 20, 1910, the patient received into the right buttock muscles 0.6 gram of "606." Aside from slight immediate pain, the patient did not have any further pain or stiffness. There was no temperature reaction. The patient was observed for four days in the hospital and subsequently by his physician. There was no change noted for the better in his mental state. On January 15 the patient was less emotional. He shows more energy and takes interest in his business affairs.

TABULAR SYNOPSIS OF THE CASES.

Case No.	Infection.	Lesion.	Treatment.	Wassermann.	Injections of "606."	Date.	Result.	Subsequent Wassermann.	Remarks.
I H. J.	4 weeks	Chancre (spirochete present) and inguinal adenitis	None	Positive (weakly)	0.6 gram alkaline solution	Dec. 20	Chancre healed on Dec. 31	Wassermann strongly positive, Dec. 31; negative, Jan. 12	On Feb. 3 no secondaries.
II R. S.	17 days	Chancre (spirochete present) (herpetic)	None	Negative	0.6 gram alkaline solution	Dec. 24	Chancre healed in 3 days	Feb. 5, negative	No secondaries Feb. 5.
III C. P.	2 months	Chancre and maculopapular syphilide and mucous patches	None	Positive	0.6 gram alkaline solution	Jan. 6	Eruption cured in 1 week Chancre cured in 2 weeks	Jan. 20, weakly positive	Patient gained 4 pounds in 1 week.
IV M. N.	2 months	Chancre (spirochete present and secondaries)	2 injections of Hg. Sal.	Positive	0.6 gram alkaline solution	Jan. 13	Chancre cured in 2 weeks Secondaries cured in 4 days	.....	Severe pain and extreme nervousness for 1 week after injection; diffuse erythematous eruption.
V J. C.	5 months	Chancre on left tonsil; mucous patches; spirochete present	None	Positive	0.4 gram neutral emulsion	Sept. 26	Cured in 1 week	Positive, Oct. 3, Dec. 19, Jan. 8	Necrosis at site of injection.
VI A. Y.	2 months	Macular syphilide; mucous patches and condylomas	None	Positive	0.4 gram neutral emulsion; 0.6 gram alkaline solution	Sept. 28 Jan. 2	Cured in 11 days Relapse Dec. 27 Cured in 40 days	Oct. 28, faintly positive; Nov. 1–7, negative; Dec. 5, positive; Jan. 8, positive	Necrosis; relapse after 2½ months; total amt. "606" = 1 gram.
VII P. E.	3 months	Maculopapular syphilide; mucous patches; iritis (spirochete present)	None	Positive	0.45 gram neutral emulsion	Oct. 8	Cured in 6 days	Oct. 29, positive; Nov. 12, positive (weakly) Feb. 5, positive (weakly)	Marked Herxheimer reaction; nerve palsies; see case history.
VIII J. M.	8 months	Maculopapular syphilide; mucous patches; condylomas (spirochete present)	Mixed treatment, few months	Positive	0.5 gram neutral emulsion	Oct. 25	Cured in 9 days	Nov. 15, positive (weakly) Dec. 24; negative; Jan. 20, positive	Rapid cure; gain of 20 pounds in 2 months.
IX F. K.	About 1 yr.	Gumma pharynx; malignant syphilis	Numerous inunctions and injections of Hg.	Positive	0.6 gram neutral emulsion	Oct. 21	Cured in 23 days	Nov. 13, positive	Case uninfluenced by Hg. and KI; cured quickly by "606"; local necrosis at site of injection.
X M. O.	2 months	Maculopapular syphilide; mucous patches; spirochete present in healing chancre	None	Positive	0.5 gram neutral emulsion	Oct. 26	Mucous patches cured in 4 days Roseola cured in 14 days	Nov. 16, positive	Gained 20 pounds in 3 weeks.

XI C. S.	15 months	Periostitis tibia	Numerous inunctions and injections	Positive	0.6 gram neutral emulsion	Nov. 1	Cured in 3 days	Nov. 11, positive; Jan. 13, positive.	
XII G. S.	Indefinite	Chancre on right tonsil; maculopapular syphilide; condylomas; mucous patches (spirochete present)	None	Positive	0.45 gram neutral emulsion; relaspe; 0.6 gram alkaline solution	Oct. 3 Nov. 10	Cured in 17 days Relapse Nov. 9 Cured in 14 days	Oct. 24, negative; Nov. 7, negative; Nov. 12, positive	Marked Herxheimer reaction, lasting 24 hours; gravid; fetus viable Nov. 10.
XIII F. G.	2½ months	Pustular syphilide; mucous patches (spirochete present); malignant case	6 injections of Hg. Cl_2	Positive	0.6 gram alkaline solution	Nov. 11	Cured in 8 days	Nov. 19, positive; Jan. 1, faintly positive	Malignant case; gained 13 pounds in 11 days; total gain, 20 pounds.
XIV C. W.	11 months	Mucous patches (spirochete present)	27 injections of Hg. Sal.	Positive	0.6 gram neutral emulsion	Oct. 5	Cured in 2 days Relapse 3 mos. later; squamous palmar syphilis	Oct. 10, positive; Nov. 1, positive; Nov. 13, positive (weaker) Feb. 5, negative	Frontal headache; dimness of vision in right eye, lasting 24 hours, day after injection.
XV H. B.	8 months	Mucous patches (spirochete absent)	70 injections of Hg.	Positive (weakly)	0.6 gram alkaline solution	Nov. 11	Cured in 4 days	Dec. 4, positive.	Relapse, Feb. 5
XVI F. K.	2 months	Intra-urethral chancre; roseola; mucous patches; spirochete absent	None	Positive	0.6 gram neutral emulsion	Oct. 7	Cured in 8 days	Nov. 30, weakly positive; Dec. 23, positive Feb. 5, positive	Small local necrosis. Relapse
XVII L. S.	1 year	Mucous patches	15 injections of Hg. Sal.	Positive	0.5 gram alkaline solution, intravenously	Dec. 2	Lesions disappeared in 2 days; death 2 weeks after injection	.....	See history.
XVIII S. M. K.	3 years	Mucous patches; no spirochete found	Hg. injection; KI	Positive	0.5 gram alkaline solution	Nov. 15	Cured within 24 hours	Positive, Dec. 1; negative, Jan. 15; positive, Feb. 1	Idiosyncrasy to Hg.; "606" well borne.
XIX P. B.	4 months	Miliary syphilide; polyadenitis	None	Positive	0.6 gram alkaline solution	Dec. 18	Syphilide disappeared in 3 weeks; adenitis uninfluenced	Positive, Jan. 12	Adenitis resistant to "606"; infiltration at site of infection.
XX S. R.	?	Pustulocrustaceous syphilide; mucous patches; periostitis	None	Positive	0.6 gram alkaline solution	Dec. 22	Mucous patches cured in 6 days Skin lesion cured (?) in 10 days	Positive, Jan. 7	Two papules on face uninfluenced by drug.
XXI H. M.	2 months	Roseola; mucous patches	None	Positive	0.8 gram paraffin emulsion	Jan. 3–Jan. 9	Cured in 11 days	Positive, Jan. 14–21	Drug given in divided doses; no pain.
XXII M. S.	6 months	Mucous patches	15 injections of Hg. Sal.; 8 injections of $HgCl_2$	Positive	0.85 gram paraffin emulsion	Jan. 3–Jan. 9	Cured in 11 days	Positive, Jan. 14	Drug given in divided doses; slight pain; lesions refractory to Hg.

TABULAR SYNOPSIS OF THE CASES—(*Continued*).

Case No.	Infection.	Lesion.	Treatment.	Wassermann.	Injections of "606."	Date.	Result.	Subsequent Wassermann.	Remarks.
XXIII M. L.	6 years	Bilateral orchitis	Numerous Hg. Sal. injections	Positive	0.6 gram neutral emulsion	Oct. 16	Cured in 6 weeks	Positive, Dec. 4	
XXIV F. P.	9 years	None	Internal and injections of Hg.	Positive	0.6 gram alkaline solution	Dec. 24	.....	Positive (weaker), Jan. 15	At patient's request before marriage.
XXV S. F.	4 years	Multiple gummas; synovitis	Prolonged Hg. Sal. injections and KI	Positive	0.6 gram neutral emulsion	Oct. 4	Cured in 20 days	Positive (weaker), Jan. 24	Case refractory to Hg.; modified Herxheimer reaction; temperature, 105.4°; follicular tonsillitis after injection.
XXVI G. P.	Indefinite	Gumma (?) of left shoulder; paralysis of both vocal cords	None	Negative	0.5 gram paraffin emulsion	Jan. 16–Jan. 18	Improved.	.....	Patient had been operated on twice; wound refuses to heal; injected at request of surgeon.
XXVII H. M.	4 years	Gumma submaxillary region	Injection of "606" at another institution 2 months ago; inunctions and injections	Negative	0.75 gram paraffin emulsion	Jan. 16–Jan. 20	Considerable improvement.	.....	Injected at request of surgeon.
XXVIII G. D.	4 years	Chronic nasal catarrh; old specific scars; deafness	Injections and KI	Positive	0.55 gram paraffin emulsion	Jan. 18–Jan. 20	Hearing greatly improved	.....	At end of 5 days could hear watch tick at 1 foot; before could not hear conversation.
XXIX J. S.	2 months	Healing chancre; mucous patches; neuritis	Internal Hg. 2 months ago	Positive	0.55 gram paraffin emulsion	Jan. 17–Jan. 23	Cured in 1 week	.....	Mercurial nephritis before "606"; urine still contains casts.
XXX A. B.	Indefinite	Paresis	Unknown	Positive	0.6 gram alkaline solution	Dec. 11	Unimproved.		
XXXI Mrs. M.	2 years	Mucous patches; headache; circinate syphilide	Inunctions and injections	....	0.5 gram alkaline solution	Dec. 12	Cured in 24 days		
XXXII R. B.	2 years	Multiple cutaneous gummas	Hg. injections	Positive	0.6 gram neutral emulsion	Oct. 26	Cured in 1 week	Positive (weak), Nov. 9	Gained 10 pounds in 2 weeks.
XXXIII I. S.	44 years	Epithelioma of tongue	None	Positive	0.5 gram neutral emulsion	Oct. 26	Unimproved	Negative, Jan. 15	Biopsy shows epithelioma; radical operation confirmed diagnosis.

XXXIV G. R.	Unknown	Gummatous ulcer of knee	Injections of Hg.	Positive (weakly)	0.6 gram neutral emulsion	Oct. 15	Cured in 5 weeks	Oct. 22, negative; Dec. 23, positive	Large necrosis at site of injection.
XXXV M. G.	Unknown	Gummas of nose, soft palate, and pharynx	Mixed treatment	Positive	0.5 gram alkaline solution	Nov. 7	Cured in 10 days	.....	Immediate improvement of pain and difficult swallowing
XXXVI M. V.	12 years	Gumma of soft palate	Hg. injections	Positive	0.6 gram alkaline solution	Dec. 7	Cured in 2 weeks	Dec. 24, positive.	
XXXVII Mrs. R.	10 years	Gummas of liver	Injections	....	0.6 gram alkaline solution	Nov. 8	Cured in 3 weeks	.....	Diagnosis confirmed by exploratory and biopsy.
XXXVIII M. D.	11 years	Tabes	Hg. injections	Positive	1.3 grams alkaline solution	Nov. 4 Nov. 22 Dec. 22	Subjective improvement	.....	Ataxia unchanged; Argyll-Robertson pupil gone.
XXXIX F. S.	20 years	Cerebrospinal lues	Hg. injections	Positive	0.45 gram alkaline solution	Nov. 25	Improved; headache gone.		
XL A. S.	4 years	Cerebral lues; incipient paresis	Hg. injections	....	0.75 gram alkaline solution and paraffin emulsion	Nov. 21 Jan. 11	Unimproved.		
XLI P. R.	4 years	Hereditary lues	Hg. inunctions; mixed treatment	Positive	0.15 gram alkaline solution	Dec. 23	Much improved.		
XLII B. S.	14 years	Hereditary lues	Inunctions, injections, and KI	Positive	0.55 gram alkaline solution and paraffin emulsion	Jan. 10 Jan. 20	Much improved.		
XLIII M. P.	11 years	Gumma of nose	Hg. for 1 year	Positive	0.6 gram alkaline solution	Nov. 14	Gumma cured in 2 weeks; relapse Jan. 11	Jan. 4, positive	Lost 20 pounds; put on Hg. injections.
XLIV S. F.	Unknown	Paresis	Numerous Hg. injections	Negative	0.6 gram alkaline solution	Dec. 20	Unimproved.		
XLV L. M.	2 years	Mucous patches	Inunctions and injections	....	0.7 gram paraffin emulsion	Jan. 21, Jan. 23	Improved.		
XLVI E. L.	20 years	Pachymeningitis	Hg. injections for 20 years	Positive	0.4 gram paraffin emulsion	Jan. 19.	Improved.		
XLVII G. S.	12 years	Squamous circinate syphilide	Hg. injections and enesol injection	Negative	0.7 gram alkaline solution	Jan. 9	Cured in 10 days	Negative, Jan. 16	
XLVIII A. K.	Indefinite	Chorioretinits in secondary	Hg. injections	Positive	0.6 gram alkaline solution	Jan. 9	Improved markedly in 10 days	Positive, Jan. 16	Feb. 7, eyesight nearly normal

THE PHYSIOLOGY OF THE PITUITARY GLAND AND THE ACTIONS OF ITS EXTRACTS.[1]

By CARL J. WIGGERS, M.D.,
INSTRUCTOR IN PHYSIOLOGY IN THE UNIVERSITY OF MICHIGAN, ANN ARBOR.

LODGED in the saddle of the sella turcica and shielded in a privileged manner from the traumatisms of the outside world, lies a small body, the hypophysis cerebri, or pituitary gland, the function of which has always been, and still is, largely shrouded in mystery. Since Galen and Vesalius taught that it filtered mucus into the nose and pharynx, the functions attributed to this gland have varied from such vitalistic conceptions as a habitation for the soul or a stopper preventing the escape of vital spirits from the third ventricle, to the more lowly duties of an excretory organ for the brain, a lymphatic gland, etc. Obviously, no scientific conception of the organ's function could be formulated until its development and structure were understood and, consequently, the discovery of its dual origin in 1838 by Rathke[2] marks the time when a beginning could be made toward the unveiling of its true function. Since then a host of histological investigators, prominent among them, Stieda,[3] Schönemann,[4] Müller,[5] Schwalbe,[7] Berkley,[7] v. Kölliker[8] Paulesco,[9] and Herring,[10] have added in a material manner to a clear understanding of its structure and development.

HISTOLOGY AND EMBRYOLOGY. The pituitary body consists of a large pink-colored anterior portion, and a smaller pale posterior part. Developmentally considered, the posterior lobe arises as a downward growth from the midbrain, its cavity being continuous with the third ventricle. This part remains permanently connected with the brain by a stalk or infundibulum, the cavity of which, except in the cat, becomes obliterated by a growth of neuroglia tissue. The anterior portion arises as an upgrowth from the buccal ectoderm, which is cut off by the fusion of the sphenoidal cartilages. At first this cut-off mass exists as a hollow island of cells, but as the cells proliferate only a cleft remains. The cells on the posterior side of this cleft apply themselves to the posterior lobe, which they cover and invade to some extent, forming cut-off masses

[1] Presented before the Detroit Medical Club, June 2, 1910.
[2] Müller's Archiv., 1838, p. 482.
[3] Ztschr. f. wissensch. Zoologie, 1868, xviii, 44.
[4] Arch. f. path. Anat. u. Physiol., 1892, cxxix, 310.
[5] Ztschr. f. Naturwissensch., 1891, vi, 354.
[6] Referred to by Herring (Ref. 8).
[7] Brain, 1894, xvii, 515; Johns Hopkins Hosp. Reports, 1895, iv, 285.
[8] "Entwickelungsgeschichte," 1878.
[9] Quoted by Parhon and Golstein, "Les Secretions Internes," Paris, 1907.
[10] Quart. Jour. Exp. Physiol., 1908, i, 121.

of cells. The rest of the cells develop into the large anterior lobe, which becomes very vascular.[11]

When fully developed, the posterior lobe is composed of neuroglia tissue, together with a few ependymal cells. Berkley believed he observed also nerve cells and fibers, but this has not been substantiated by subsequent investigators, and it seems probable, as Herring points out, that the cells described as nerve cells were in reality not such. The posterior lobe has an epithelial investment, first described by Peremeschko,[12] in 1867, but more in detail by Paulesco, in 1906, and Herring, in 1908. According to this latter observer, the completeness of this epithelial covering varies in different animals. In the cat and dog the investment is complete, but in most mammals (man, monkey, ox, pig, rabbit) the epithelium does not entirely surround the posterior lobe, but is more particularly gathered toward its anterior part, forming the pars intermedia of the pituitary gland. A few gland cells are seen scattered here and there throughout the neuroglia tissue. This part is almost devoid of bloodvessels, and the colloidal secretion (or degeneration products?) of the epithelial cells is passed into the neurogliar tissue to be absorbed, by its lymphatic system, into the third ventricle.

The anterior lobe consists largely of differentially staining, granular cells, that are arranged in columns around thin-walled blood spaces. No evidences of glandular ducts are present. Haller[13] claims that the anterior lobe is a tubular gland, discharging its secretion directly into the subdural space, but the evidence of other histologists appears against such a view, and indicates rather that these cells discharge their secretion directly into the blood spaces.

The Functions of the Pituitary Gland. One of the first questions of interest in studying a gland's function is its necessity to life. Physiologists and surgeons alike have attempted to answer this question by determining the effects of its removal. In 1892 Marinesco[14] reported that removal of the pituitary gland in cats was fatal within one to eighteen days after the operation. Before death the animals showed signs of emaciation, a fall in temperature and heart rate. Vassale and Sacchi[15] reported that the removal of the pituitary gland in forty animals (cats and dogs) resulted in death within five to seven days. The symptoms before death consisted in an accelerated respiration (amounting at times to dyspnœa), polyuria, polydipsia, vomiting, rigidity of the posterior limbs, fibrillary twitchings and clonic as well as tonic convulsions. Partial removal caused less pronounced symptoms, and occasionally the animal survived. Similar results have been reported by Casselli.[16]

[11] For excellent diagrams see Herring, Quart. Jour. Exp. Phys., i, 121.
[12] Arch. f. path. Anat. u. Physiol., 1867, xxxviii, 329.
[13] Morpholog. Jahrb., 1896, xxv, 101.
[14] Compt.-rend. Soc. de biol., June, 1892.
[15] Arch. ital. de biol., 1893, xviii, 3.
[16] Quoted by Parhon and Golstein (loc. cit.).

In 1900 Friedmann and Maas[17] reported that extirpation of the pituitary gland was compatible with life. Lo Monaco and Van Rynberk,[18] in 1901, Gaglio[19] in 1902, and Pirrone[20] in 1903, also came to this conclusion. They admitted that serious symptoms and even death often followed its removal, but attributed these unfortunate events to cerebral traumatisms or infections. The fact that some animals survived fifty to eighty days was advanced as proof sufficient that the gland was not of vital importance. In 1905 Fichera[21] found that partial removal of the gland in pullets caused, not death, but a stunted growth. He could not be certain, however, that the effects were not due to cerebral injury.

Experimenters were thus divided into two camps, the one group believing that the gland was of vital importance, suspicioned an incomplete removal in case death failed to occur; the other group holding that it was not necessary to life, attributed the symptoms and death to cerebral injury and infection. This was the state of affairs in 1906 when Paulesco[22] devised the technique for the temporal route of reaching the pituitary body, a method that possesses at least two advantages, viz.: it permits the removal of the gland *de visu* and minimizes the risk of infection or traumatism. Paulesco[23] reported that complete removal by this method was invariably fatal, but that partial removal was compatible with life if the part remaining contained some of the anterior or epithelial portion. Cushing,[24] in this country, has been able by the use of this method to substantiate that ablation of the anterior lobe is always fatal in adult canines, but that removal of the posterior lobe is entirely without effect. Crowe and Cushing[25] point out, however, that young animals survive a total hypophysectomy longer than adult ones. Crowe, Cushing, and Homans[26] have strengthened these results by being able to ward off death and the serious symptoms caused by total extirpation of the gland, by its transplantation into the brain substance or the red bone marrow of long bones.

Not only is the gland necessary to sustain life, but clinical men and pathologists have also added evidence which indicates its importance to normal functions, for, when the anterior lobe becomes hypertrophied or atrophied (implying increased or decreased secretion), certain developmental disturbances apparently arise which vary in degree at least with the age at which they occur. Thus, a congenital hypertrophy of the pituitary gland is frequently asso-

[17] Berl. klin. Wchnschr., 1900, p. 1213.
[18] Quoted by Parhon and Golstein (loc. cit.).
[19] Arch. ital. de Biol., 1902, xxxviii, 177.
[20] Quoted by Parhon aad Golstein (loc. cit.).
[21] Ibid.
[22] Report at Acad. des science., June, 1907; "L'Hypophyse du Cerceau," 1908.
[23] Loc. cit.
[24] Proc. Amer. Physiol. Soc., Amer. Jour. Physiol., 1908, xxiii, 23.
[25] Jour. Amer. Med. Assoc., 1909, liii, 247.
[26] Quart. Jour. Exp. Physiol., 1909, ii, 389.

ciated with a general overdevelopment of the body (giantism), whereas an hypertrophy occurring in adult life apparently gives rise to acromegaly, a condition characterized by greatly overdeveloped extremities. Congenital hyposecretion causes infantilism, whereas later in life it is followed by a loss of sexual characteristics. These altered states of secretory activity may be induced by various causes, some but imperfectly understood. The compression of the pituitary by tumors, the effect of blood supply and nutrition and of the products elaborated by other glands of internal secretion on the pituitary are still awaiting more detailed investigation and need concern us here no further.

The following facts, then, seem established: (1) The pituitary gland is necessary to life, and any diminution or increase in its function results in metabolic or sexual disturbances; and (2) this control over the body is probably exerted through an internal secretion elaborated *by the cells of the anterior lobe.*

Nature of the Internal Secretion. Has the internal secretion been determined? What is its natrue? Is it a single substance or does the gland secrete a number of substances? Answers to these and similar questions have been sought by studying the effects of injections of its extracts on the muscular and nervous functions, on nutrition and development, on the secretion and composition of urine, on the flow of the digestive juices, and on the cardiovascular system, this latter supplying the most productive field for research.

Experimentation has shown that by water, glycerine, or salt solutions, a substance may be extracted from either fresh or dried glands which resist boiling, and, when introduced intravenously or intraperitoneally, causes polyuria, slow or accelerated pulse, accelerated respiration, dyspnœa and motor disturbances, such as ataxia and paralysis of the hind legs, symptoms, it will be noted, which are also characteristic of the removal of the gland. This substance is obtained only from the posterior lobe, however. The extracts thus far obtained from the anterior lobe are apparently inert even when injected in enormous doses.[27] This fact seems very peculiar since it is the anterior lobe which is composed of glandular tissue and which would, therefore, be expected to furnish the physiologically active principle, and the paradox becomes still more interesting when we consider that it is this portion alone which is of vital importance.

The fact may receive several interpretations. We may imagine that the active substance is secreted by the anterior lobe in an inactive form and that it becomes activated or chemically altered in some manner as yet not understood after reaching the posterior or neurogliar portion. Schäfer[28] apparently leans toward such a view. This hypothesis, nevertheless, requires a brave assumption, since,

[27] L'Hypophyse et la Medication hypophysaire, Paris, 1909.
[28] Philosoph. transact. B., cic, 1.

first, no proof exists that neurogliar tissue possesses such an activating or formative power; and, secondly, there is no evidence that the anterior lobe passes its secretion into the posterior lobe—in fact, histological evidence appears opposed to it. For this reason, it seems to me, we are not justified in assuming that the substance extracted from the posterior lobe is identical either in composition or action with that of the anterior lobe. Until further evidence is forthcoming, I prefer to believe that this lobe elaborates a secretion as yet unknown, which affects nutrition and is necessary to life, and that the posterior lobe either forms an additional secretion not of vital importance, or contains chemical substances which, though not normally secreted into the blood, when extracted and introduced, affect the body functions. The reasons for my belief, summarized, are: (1) The anterior lobe alone has an influence on growth, development and life, whereas the extracted substance is found only in the posterior lobe; (2) there is no evidence of the extracted substance in the normal circulation; and (3) injections of the extract do not neutralize the symptoms arising from extirpation of the gland, but, in large doses, they produce symptoms that simulate them.

For the present, then, it seems preferable to regard *extracts of the pituitary gland* rather as drugs which exert a characteristic action on the body than as physiological secretions—drugs whose therapeutic value consists of the effects they may produce on the heart, bloodvessels, kidney, etc., rather than of any hypothetical value they may possess in supplementing a deficient function of the anterior lobes.

THE ACTIONS OF PITUITARY EXTRACTS (SOME UNSETTLED PROBLEMS). A perusal of the literature indicates that the effect of pituitary extracts, even on the circulatory system, where it has been most extensively studied, is by no means universally agreed upon. To expedite an analysis of its action, I have summarized the literature on its circulatory effects and in the discussion propose to add a number of results that I have recorded while using pituitary extract in investigating other problems (Table I).

TABLE I.—*Summary, Circulatory Effects of Pituitary Extracts.*

Investigator and date.	Portion used.	Solvent or extractive.	Effect on blood pressure.	Effect on heart rate.	Effect on amplitude of beat.	Action on bloodvessels.	Remarks.
Oliver, Schäfer, 1895	Entire gland	Water, glycerine	Increased	No slowing	Increased	Constriction	
Howell, 1898	Anterior lobe	Water, glycerine	No effect	No effect			Vagotomy modified slowing
	Posterior lobe	.....	Increased	Slowed	Increased or decreased	Constriction	
Livon, 1898	?	Glycerine	Increased	Slowed	Increased	.....	Vagotomy prevented slowing
Schäfer, Vincent, 1899	Anterior lobe	Saline	No effect	No effect			
	Posterior lobe	.....	Increased; on 2d or 3d injections decreased	No effect or slowed	Increased	Constriction	Vagotomy abolished slowing
	Posterior lobe	Alcohol	Decreased				
de Cyon, 1899–1900	Entire gland (?)	Saline	Increased	Slowed; periodic rythm	Increased	Constriction	Slowing not entirely prevented by atropine or vagus section
		Alcohol	Fell	Slowed	Increased	Dilation	
Osborne, Vincent, 1900	Posterior lobe (outer part)	Salt solution	Negative				
	Posterior lobe (inner part)	Salt solution	Increased	Slowed or no effect			
Hamburger, 1904–1910	Anterior lobe	Saline, alcohol, glycerine	Decreased	Increased	Decreased		
Silvestrini, 1905	Anterior lobe	Salt solution	Negative				
	Posterior lobe	Salt solution	Temporary increase	.....	Increased		
			Later, decrease	.....	Later decreased		
Garnier, Thaon, 1906	Anterior lobe	Salt solution	Negative				
	Colloid at anterior lobe	Salt solution	Negative				
	Posterior lobe	Salt solution	Increase Later decreased	Slowed	Increased Weaker	.....	Vagotomy prevents slowing
Schäfer, Herring, 1906	Anterior lobe	Saline	Negative				
Hallion, Carrion, 1907	Entire gland (?)	Saline	Increased	Slowed	.....	Constriction, later dilation	
Schäfer, Herring, 1908	Epithelial portion posterior lobe	Saline	Increased Decreased on subsequene injection	Slowed or no effect Often temporary acceleration	.....	Constriction	
	Neuroglia portion	Saline					
	Same	Alcohol	Negative				
de Bonis, 1908	?	?	Increased	Slowed	Increased	.....	Slowing not abolished by vagotomy
Halliburton, Candler Sikes, 1909	Posterior lobe (human pituitary)	Saline	Increased	No effect			

Effects on Bloodvessels and Arterial Pressure. Experimenters are commonly agreed that pituitary extracts cause a rapid and pronounced increase in blood pressure, different from that of adrenalin in its longer duration. This rise is largely due to a constriction of the arterioles, for, as shown by Oliver and Schäfer,[29] Howell,[30] and later by Schäfer and Vincent,[31] the size of organs such as the intestine, spleen, and limbs diminish concomitantly with the elevation of pressure. The constrictor action is chiefly peripheral, for, as Oliver and Schäfer, and also Howell, have demonstrated, it occurs after destruction of the medulla and spinal cord. Furthermore, Oliver and Schäfer found that it decreased the flow through a perfused frog. More recently, Magnus and Schäfer[32] have supplied evidence that not all the peripheral vessels are affected equally, and have pointed particularly to the frequent and prompt increase in size of the kidney when the pressure rises, an effect directly opposite to that produced by adrenalin. While investigating the relative value of vasomotor drugs in renal hemorrhage,[33] I had occasion to substantiate this fact, and further, to show that the venous outflow from this organ was markedly augmented after administration of pituitary extract. These results indicate either that the rise in pressure passively overpowers the local constriction or that the drug exerts a direct dilator action on the renal vessels as well. I have a number of times perfused the drug through the kidney of a dog and when thus tested invariably caused a constriction, as shown by a decreased outflow and an increase in the height of the oscillatory perfusion pressure. The constriction induced by the extract obtained from $\frac{1}{10}$ gram of fresh infundibulum corresponded in degree to that resulting from 1 c.c. of a 1 to 100,000 solution of crystalline adrenalin. From this it differed, however, by being *of shorter duration* and unmodified, as far as I have been able to determine, by a dose of apocodein or of ergotoxin sufficient to abolish completely the action of adrenalin. Should subsequent experiments corroborate this observation, it would indicate that the drug acts directly on the muscle and not on the nerve endings in the bloodvessels, as is the case with adrenalin. In a few cases the constriction induced by pituitary extract was followed by a dilation such as I have previously reported following the constriction of chloroform. Such a dilation has not only been obtained with the commercial preparation "Pituitrin," in which the chloretone preservative might possibly be suspected of being responsible for the dilation, but with a saline extract of the fresh infundibular portion containing no preservative. It is not impossible that a larger series of perfusion experiments

[29] Jour. Physiol., 1895, xviii, 277.

[30] Jour. Exp. Med., 1898, iii, 248.

[31] Proc. Physiol. Soc., Jour. Physiol., 1899, xxiv; Proc. of Soc., p. xix; Jour. Physiol., 1900, xxv, 87.

[32] Jour. Physiol., 1901, xxiii; Proc. Soc., 9.

[33] Arch. Int. Med., 1910, v, 348.

on various organs may show this dilation frequently to follow the preliminary constriction thus indicating that the increase in the kidney volume observed in animal experiments is not entirely a passive affair. Sollmann has also shown that pituitary extract has a slight central dilator action, for when the spleen left in contact with the central nervous system was perfused, an intravenous injection caused a slight dilation of the splenic vessels.

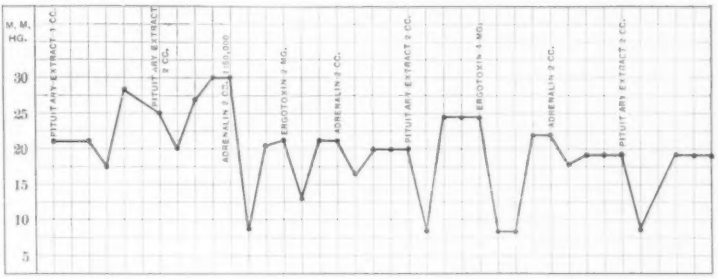

FIG. 1.—Plot showing action of pituitary extract and adrenalin when perfused before and after ergotoxin.

Action on the Heart. Most experimenters have come to the conclusion that pituitary extract slows the heart and increases the amplitude of its contractions, but the details are more or less at variance. Oliver and Schäfer[34] in their first report observed no changes in heart rate, but Howell[35] described a slowing which occurred synchronously with the main rise in pressure. Schäfer and Vincent[36] subsequently observed this slowing, but found it entirely absent in a certain number of cases. When it did occur, it was usually not coincident with the rise of pressure, but occurred after the pressure had passed the highest level. Not infrequently, too, it was preceded by a period of acceleration. Similar differences in results are also evident in the reports and curves of other investigators. In addition to a slowing, de Cyon[37] and Garnier and Thaon[38] noted changes in the rhythm of the heart, the beats grouping themselves into periods of two or more.

The causation of the slowing is also unsettled. According to Livon,[39] Garnier and Thaon,[40] and Schäfer and Vincent, it is apparently due to a stimulation of the cardio-inhibitory centre, since it is abolished by vagus section. According to Howell and de Cyon it is at least only partly due to this, for, while the cardiac action may

[34] Loc cit.
[35] Loc cit.
[36] Loc cit.
[37] Arch. f. d. ges. Physiol., 1898, lxxiii, 339; 1900, lxxxi, 94.
[38] Jour. de physiol. et de path. gén., 1906, viii, 251.
[39] Jour. de physiol. et de path. gén., 1909, ix, 16.
[40] Loc cit.

be modified by the section of the vagi, or by injection of atropin, slowing is not prevented. They, therefore, concluded that pituitary extracts exert a direct effect on the heart as well. Support is given to this view by the fact that the same slowing occurs, as I have found, when the drug is perfused through a rabbit's heart isolated from all nerve centres. In such experiments the peculiar grouping of beats was also occasionally present.

As far as the effect of intravenous injections on heart rate is concerned, I find that my records of twenty-seven injections consist of a miscellaneous series of results corroborative of nearly every worker. The same pituitary extract (Pituitrin, P., D. & Co.) was employed in all of these cases.

TABLE II.—*Effect of Pituitary Extract on Rate and Contraction of Heart.*

Experiment.	Dose pituitrin.	Rate per 10 sec.			Amplitude in mm.			Remarks.
		Before.	During pressure rise.	1 minute after.	Before.	During pressure rise.	1 minute after.	
327	2 c.c.	21	..	17	18	18	17	
329	2 c.c.	17	..	15	11	12	9	
330	2 c.c.	18	..	15	16	16	14	
	4 c.c.	17	..	15	16	16	14	
333	2 c.c.	20	**23**	20	12	**16**	11	
335	2 c.c.	29	29	24	20	*18*	15	
334	2 c.c.	31	..	30	18	..	13	After hemorrhage
339	4 c.c.	34	*30*	21	24	**26**	9	Vigorous artificial respiration
341	2 c.c.	27	27	20½	10	**12**	11½	After hemorrhage
355	2 c.c.	18	*17*	18	22	*20*	19	
	3 c.c.	18	18	18	14	14	13	
	4 c.c.	16	**17**	16	14½	14½	14	
360	4 c.c.	16	*15*	15½	25	25	27	
361	3 c.c.	23	*22*	20	17	*14*	15½	
	3 c.c.	22	22	22	17½	**18**	18½	After atropine, 1 mg.
	4 c.c.	17	*16*	16	17	**18**	16½	
362	3 c.c.	18	**21**	14	20	**21**	19½	
	3 c.c.	19	**20**	14	20	*18*	16½	After previous dose of digitalis

Upon grouping these experiments, I find: (1) Cases in which no slowing follows the injection (cf. 335, 334, 333, 361); (2) cases in which an immediate slowing takes place which is usually continued (cf. 339, 355, 360, 361); and (3) cases in which the slowing is late in its onset and sometimes preceded by an acceleration (cf. 333, 362).

To explain and harmonize these results and the effects of vagus section on them, I have formulated the following tentative hypothesis, which fits in with the data so far in hand but which future work may not substantiate. *The slowing of the heart occurring synchronously with the rise in pressure is due to a stimulation of the cardio-inhibitory centre. The slowing which is late in its onset is due to a direct action on the heart.* Either, both, or neither of these

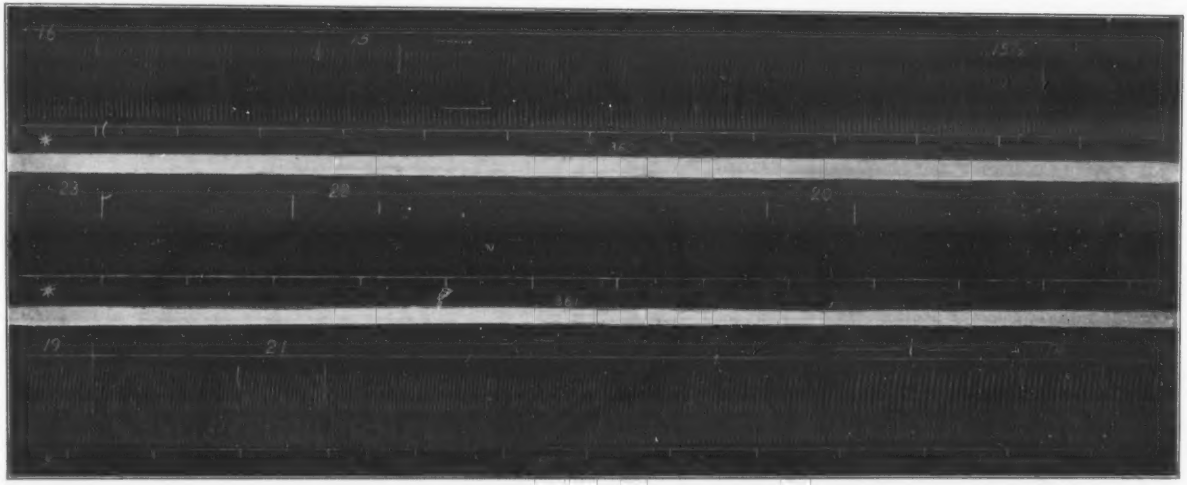

FIG. 2.—Three cardiographic tracings from different dogs, showing effect of 2 c.c. "pituitrin" injected at *. Upstroke, systole. Figures indicate heart rate per ten seconds. Upper curve shows temporary increase in amplitude followed by decrease, slight but immediate slowing (vagus action?). Middle curve shows an early decrease in amplitude, systole decreased, tonus increased. Slight early slowing (vagus action?), more pronounced later (direct cardiac action). Lower record shows very temporary increase in amplitude followed by a decrease. Heart rate first accelerated, later markedly slowed (direct cardiac action).

actions may follow the injection of pituitary extract, the factors determining the reaction being unknown. If both effects are present, vagus section will modify but not abolish the slowing. If the slowing is due to a vagus action alone, vagotomy will prevent the slowing, while, if late in its onset, and due to a depressing cardiac action, it will exert no influence.

It is quite generally assumed that pitutiary extract increases the amplitude of contraction, an assumption which, in the majority of cases, it appears, is unfortunately based on no other evidence than the size of the oscillations of a blood pressure tracing which, of course, is no criterion of the strength of the beat. Oliver and Schäfer[41] alone, so far as I have been able to discover, obtained myographic tracing of the heart. They concluded that these records showed an increase in the amplitude of contraction. Hebdom and Cleghorn[42] obtained, on perfusing the apex of a dog's heart with extracts of the posterior portion of the pituitary gland, only a decreased amplitude of contraction, which was the rule in my own experiments. The tracings published by Osborn and Schäfer likewise show clearly that the augmentation of ventricular contraction is rather fleeting and followed by decrease in strength. With this discrepancy in mind, I carefully analyzed my own curves of the ventricular contraction recorded by a cardiograph, and in a few instances by a cardiac plethysmograph. The results of a number of these experiments I have also incorporated in Table II. They show that in 85 per cent. of experiments a decrease in amplitude of contraction, similar to that observed in the perfusion experiments, occurred. It took place synchronously with the late slowing in both cases. I therefore believe that pituitary extracts exert a late depressing action on the strength of beat as well as the rate of the heart. In a number of experiments, 20 per cent., this depression (which I consider the characteristic cardiac action) is preceded by a brief period of strengthened beat, sometimes accompanied by a slight acceleration and occasionally by a slight slowing.

The Dissimilarity of Adrenalin and Pituitary Extract. Both adrenalin and pituitary extract cause a rise in blood pressure, and for that reason the statement is often made in pharmacological literature that the two substances cause similar reactions. My results indicate that such a statement is not warranted. The likeness of the two reactions ceases with the rise in blood pressure, and, as regards its other actions, no two drugs could be more dissimilar. A comparison of the reaction of the two drugs may be made from the following summary:

[41] Text-book of Physiology, i, 947.

[42] Scand. Arch. f. Physiol., 1897, viii, 163; Amer. Jour. Physiol., 1899, ii, 273.

	Adrenalin	Pituitary Extract
Blood pressure	Rapid rise Temporary	More gradual rise Prolonged
Heart rate (Vagus intact) (Vagus cut)	Slowed chiefly by vagus action Accelerated Rarely slowed	Slowed chiefly by direct depressing action Slowed Rarely accelerated
Heart strength (Intact or perfused)	Increased systole Decreased tonus Amplitude increased	Decreased systole Increased tonus Amplitude decreased
Renal vessels	Constricts only Abolished by apocodein and ergotoxin	Constriction may be followed by dilatation Not affected by either

Number of Active Substances in Pituitary Extract. Since the pituitary extracts affect gland, nerve, and muscle cells as well as the heart and bloodvessels, and since no single chemical substance has been isolated, as is the case with adrenalin, it is not impossible that they contain more than a single active substance. The first suggestion that pituitary extract contains more than one chemically active substance was made by Schäfer and Vincent. These investigators pointed out that, although the first injection induced a rise in blood pressure, subsequent doses are less and less effective and may even cause a fall. Hence, they concluded that pituitary extract contained a pressor and depressor substance having opposite effects on the bloodvessels; that, in the case of the first injection, the pressor substance overpowered the depressor and, as tolerance developed, the latter substance alone remained active. At first, these investigators believed that they were able to extract the depressor principle with alcohol and ether, but in his most recent publication Schäfer explains this result as due to an imperfectly absolute alcohol. The depressing principle suggests cholin as far as its action on the blood pressure is concerned, but, according to Schäfer and Vincent, this substance acts on the heart, while they apparently attribute the action of the depressing pituitary substance to a dilator action on the bloodvessels. As we scan the curves reproduced by various workers, we many times obtain a suggestion of a fall in blood pressure, especially when more than a single dose has been administered. This may be attributed to a depressor principle, but unless accompanied by cardiographic records, such curves are difficult to interpret. In some cases, where I obtained a similar diminution, this fall was clearly due to a depression of the heart by pituitary extract, and not a vasodilation. At first thought the dual action on the perfused renal vessels might seem to supply evidence of two substances—a constrictor and a dilator. Even if subsequent experiments should indicate that a large percentage of perfused kidneys give such a reaction, this assumption need not be made, for, as I have shown before, a single chemical substance like

chloroform may cause such a double action. Furthermore, the constrictor reaction of the perfused kidney does not diminish on subsequent injection, much less is it supplanted by a dilation. Hence, further evidence is demanded before we can assume the existence of two principles affecting the peripheral vessels.

A second suspicion of two substances in pituitary extract was voiced by de Cyon, who believed he had isolated a substance (hypophysine) in alcoholic and ethereal extracts which acted to slow and augment cardiac contractions, while the residue extracted with water caused no cardiac effect but constricted the bloodvessels Schäfer and Herring, however, on repeating similar experiments could not find any active substance in alcoholic extracts, nor could they find any difference in activity between saline extracts from fresh glands and from the residue left after previous extraction with alcohol and ether. Thus, the proof of separate substances acting on the heart and on the bloodvessels does not seem clearly established.

More recently, Schäfer and Herring came to the conclusion that pituitary extract contained a substance with a specific action on the renal cells. They based their contention on the fact that, although repeated doses of pituitary lose their pressure-raising ability, they retain their ability of promoting urinary secretion. Houghton and Merrill,[43] however, were not able to satisfy themselves that any diuresis occurred which could not be satisfactorily explained by the blood pressure changes.

Similarly, Pemberton and Sweet[44] believe that extracts of pituitary contain a substance capable of inhibiting the flow of pancreatic juice through action on the cells, but Edmunds[45] maintains that no inhibition occurs except as it is induced by changes in the blood supply. It is evident, then, that more convincing work will be necessary before we may safely assume the existence of more than one principle in extracts of the pituitary gland.

SUMMARY. In conculsion, it may be well to recapitulate briefly the chief ideas that I have sought to bring out in this paper.

1. Developmentally and histologically, the pituitary gland is composed of an anterior or epithelial portion and posterior or neurogliar portion.

2. The anterior lobe evidently elaborates a secretion that is necessary to life and to normal metabolism and development.

3. This substance has so far resisted extraction by various solvents, hence its chemical nature and physiological properties remain unknown.

4. The posterior lobe, which is not of vital importance, contains or secretes a substance that may be extracted by water, glycerine, or

[43] Jour. Amer. Med. Assoc., 1908, li, 1849.
[44] Arch. Int. Med., 1908, i, 634.
[45] Jour. Pharmacol. and Exp. Therapeut., Proc. of Society, 1909, i, 571.

salt solution, and resists boiling, but it has not been demonstrated that it is identical with the secretion of the anterior lobe or that it represents its vital principle.

5. These extracts constrict the peripheral vessels (probably by a direct muscular action), thus producing a marked rise of arterial blood pressure. This constriction is not equally pronounced in all organs, for the renal vessels are, at least passively, dilated during its action.

6. These extracts are generally stated to slow and strengthen the heart, but myographic tracings of the intact and perfused heart indicate a depressing influence to be the most constant and characteristic one, an increase in the amplitude being only exceptionally the case. The slowing, as well as depression, are largely attributable to a direct cardiac action, but the former may be augmented by a vagus effect.

7. Pituitary extract resembles adrenalin in its action only in that it causes a rise in blood pressure. The manner in which they affect the heart and bloodvessels, as well as the effects induced, are entirely different.

8. In addition to its cardiovascular actions, pituitary augments the secretion of urine and inhibits the flow of pancreatic juice, but it has not been definitely determined whether these varied reactions are due to separate substances, to a specific affinity of a single substance for different cells, or whether they are secondary to changes in the circulation.

STIFF AND PAINFUL SHOULDERS, WITH LOSS OF POWER IN THE UPPER EXTREMITY.[1]

By T. Turner Thomas, M.D.,

ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL, PHILADELPHIA.

Most physicians of experience have had patients with persistently stiff and painful shoulders and weakness of the arm, usually following some trauma to the shoulder, but sometimes without any history of such a cause, and they have been at a loss how to account for or to treat them. The complaints of the patients vary somewhat, but they are sufficiently similar to warrant the suspicion, at least, that most of them are due to a common cause, although some cases deviate from the usual type enough to raise the question of a common origin and to make the solution of the problem

[1] Read at a meeting of the Northwestern Medical Society of Philadelphia, September 5 1910.

a difficult one. It is very likely that the different stages in which the condition is met with by the physician, the varying nature of the injury causing it or the absence of any definite history of associated injury, the radiation of pain along one or more nerves or its localization in the region of the shoulder or at some other place, and the degree of atrophy present in the surrounding muscles have been responsible for the variety of terms under which conditions having probably a common pathological basis are diagnosticated. Many of them have been looked upon as rheumatic, and I believe that rheumatism can be responsible for it, although most of them are undoubtedly traumatic. Cases seen after dislocations or fractures about the shoulder, in which the limitation of movement is marked, have been called "fibrous ankyloses." It is very probable that the loss of power in the muscles, particularly in the deltoid, in large part due to the atrophy of disuse, has passed for a "paralysis of the deltoid." Undoubtedly many of those in which the pain radiates to the insertion of the deltoid, to the elbow or forearm, have been wrongly diagnosticated as cases of "neuritis." Often in such cases, if there is limitation of movement in the shoulder, it is slight and not easily recognized on account of the associated movement of the scapula. In one case a prominent surgeon made the diagnosis of traumatic arthritis, on account of the prolonged pain and stiffness in the shoulder. This patient, while riding in a street car with his well arm carrying parcels, managed to raise the hand of the affected side high enough to catch a strap with which to steady himself. The car suddenly gave a lurch, unbalancing the patient in such a way that the strap hand was compelled to support his whole weight. There was a sudden snap in the shoulder, with severe pain, but from that moment, the patient says, the stiffness of the shoulder disappeared and some time later the pain, so that gradually the shoulder returned to its normal condition. It is very unlikely that such an accident would have cured a traumatic arthritis.

The one feature that characterizes the cases which I have chosen for discussion is a more or less marked limitation of abduction and rotation in the shoulder-joint, never complete but usually crippling and very persistent. In the early stages there is always acute pain about the joint, often radiating to the arm, sometimes to the forearm, or even to the hand. There is loss of power in the muscles of the shoulder and arm not readily accounted for entirely by the pain on motion. Indeed, in the later stages there may be little or no pain, although even then there will usually be pain if the restricted motion is forced. When the pain in the shoulder has disappeared, it is frequently found to radiate down the arm, often about the insertion of the deltoid. Scapulohumeral limitation of movement is always present in some degree. Jarjavay, in 1867, and Duplay, in 1872, accounted for the condition by

assuming the existence of a periarthritis, which localized itself particularly in the subdeltoid or subacromial bursa. More recently Küster,[2] in Germany, and Codman,[3] in this country, have again called attention to the importance of an inflammation of this bursa in the causation of these stiff and painful shoulders.

Codman's work has received wide attention in this country, and it may be said that his conclusions have been generally accepted. For some time I have entertained a conception of the pathology of these cases, which differs decidedly from that based upon the bursitis theory, and so far as I am aware it has never been offered before. I believe that we have to do with a periarthritis in these cases, but not of bursal origin. Whoever would hope to attract any attention to a new theory must recognize the fact that no other has seemed to account so well for the wide variety of symptoms and associated conditions, as that based upon an inflammation of the subdeltoid or subacromial bursa. In my opinion, Codman's paper is the strongest we have on the subject, in that it presents positive evidence of firm bursal adhesions in a considerable number of cases operated on and cadaver specimens. In one cadaver specimen, with the typical limitation of movement, even after the division of all the muscles of the shoulder and the anterior part of the capsule, the subdeltoid adhesions alone maintained the limitation of abduction and external rotation. Yet, notwithstanding the evidence produced by Codman, there is still room for discussion as to the pathology of this condition, and I am disposed to regard the bursitis theory as not proved. The one cadaver specimen, in which it was demonstrated clearly that the subdeltoid adhesions were responsible for the scapulohumeral ankylosis, merely indicated, I believe, that there had been an unusual inflammation in the bursa in this case. As for the others, the cadaver cases and those operated on, I do not believe that the fibrous bands found account for the resistance to the force which is necessary to overcome the limitation of motion. There are other reasons why they probably do not, but I wish to call attention here to one objection to this theory, drawn from Codman's paper. He says: "In some of these cases which are etherized and manipulated the adhesions may be felt to tear, sometimes with alarming violence, so that one suspects fracture of the humerus or rupture of the internal lateral ligament of the elbow." In one of my cases I thought that I had surely torn some ligament at the elbow, and in another the same sensation was observed to a milder degree. In this second case there developed in a few days a distinctly localized area of ecchymosis over the internal condyle, indicating that something had been torn there. Codman believes that the tearing

[2] Archiv f. klin. Chir., 1902, lxvii, 1013.
[3] Boston Med. and Surg. Jour., 1906, cliv, 613.

at the shoulder occurs in the subdeltoid and subcoracoid bursæ, possibly also in the older cases in the substance of the contracted and and shortened subscapularis muscle, and that the tearing sensation over the internal condyle occurs simultaneously with and is due to the tearing at the shoulder. He says, further: "In six cases I have made an incision into the bursa on the point of the shoulder between the fibers of the deltoid, and have torn the adhesions with my fingers *before using the leverage with the arm.* In two cases it was necessary to divide the adhesions with scissors." He clearly implies that it is the leverage with the arm that produces the alarming tear, which suggested the rupturing of the internal lateral ligament of the elbow, even after the adhesions in the bursa have been thoroughly broken by the fingers or divided by scissors. Where is the resistance that calls for such force after the subdeltoid adhesions have been removed? Surely not, as suggested by Codman, in the small, delicate subcoracoid bursa, which is sometimes absent. If the shoulder can perform its normal function without this bursa, then adhesions in it will not interfere much with its movement.

I have dissected this bursa eight times, four times after injecing it with plaster of Paris. Except the subscapular, it is the largest of the bursæ about the shoulder, of which some anatomists enumerate as many as ten. I cannot agree with Codman and Küster in regarding it as a very extensive and complicated serous sac. Küster says that it extends above deeply under the acromion, below over the greater part of the anterior joint region, between the deltoid muscle and the joint capsule, and externally reaches as far as the greater tuberosity. I observed that in every one of my specimens, except one, it was circumscribed to the upper surface of the greater tuberosity (Fig. 1), and to a small portion of the supra- and infraspinatus tendons inserting into the tuberosity. In one specimen it extended somewhat farther inward toward the coracoid process (Fig. 2). When the arm is at the side of the body and the forearm across the front of the chest, the greater tuberosity lies in front of the acromion process, the bursa then being covered by the corresponding portion of the deltoid, the fibers of which are here very thin and the greater tuberosity easily palpable under it. Only a small part of the bursa extends under the acromion, about a half inch (Fig. 2). It is very simply constructed, with regularly defined borders, and it is slightly elongated anteroposteriorly. It has a diameter of approximately two or two and one-half inches. With the overlying deltoid removed, as the head of the humerus is rotated externally, the bursa is seen to move with it because it is firmly adherent to the tuberosity, and as it moves gradually changes its shape, becoming smaller. In full external rotation, the subdeltoid portion, *i. e.*, the portion exposed beyond the edge of the acromion, is very much smaller than in internal rotation (Fig. 3). The subdeltoid portion is now external

to the acromion, and if the arm is abducted to an angle of 45 degrees it becomes almost entirely subacromial. It always follows the

FIG. 1.—Front view. Bursæ injected with plaster-of-Paris. Both arms in sling position (adduction and internal rotation), except for slight abduction in right. Both bursæ anterior to acromion and extending about one-half inch under it. Right about normal size, left about one-third larger from forced injection.

FIG. 2.—Lateral view from above. Bursa overdistended from forced injection. Effect of the exposure to camera is to make bursa appear relatively larger than in actual specimen. It is, however, wider than in any other of the eight specimens examined. It extends under the whole length of the coraco-acromial ligament to the coracoid process. It is probably continuous with the subcoracoid bursa. The extent of the subacromial portion in this position of the arm is fairly well indicated.

greater tuberosity, which is now under the acromion almost entirely (Fig. 4). It is evident that its attachment to the overlying deltoid must be very loose to permit so great movement of the bursa under the muscle, and so great a change in its shape. The wall of the

FIG. 3.—Right arm of specimen shown in Fig. 1, is in full external rotation. The bursa carried by the greater tuberosity to which it is attached, is now external to the acromion and is slightly diminished in size.

FIG. 4.—Same specimen as in Figs. 1 and 3. Right arm in full external rotation and abducted to an angle of about forty-five degrees. Bursa almost entirely under acromion.

bursa is exceedingly thin, of tissue paper thinness. There must be a very decided change in its thickness and in the firmness of its attachment to the overlying deltoid before it can offer the resistance to movement which is found in the cases under discussion.

The resistance from bursal adhesions can be no stronger than the bursal walls.

The position of rest in the shoulder after an injury, or when the joint is inflamed, is with the arm in adduction and internal rotation. The limitation of movement is from this position, *i. e.*, into abduction and external rotation. With the arm in the position of rest, the bursa is almost entirely subdeltoid and directly in front of the acromion, over the greater tuberosity and under the thin portion of the deltoid, where the tuberosity is easily palpable. It is evident that if the bursal adhesions are to limit the movement of the humerus, the normally loose upper bursal wall must have become firmly fixed to the overlying deltoid by new and dense cicatricial or inflammatory tissue. Under such circumstances, if there were any movement of the greater tuberosity it could only be by dragging with it the adherent deltoid, which is here so thin that movement of it could easily be recognized by its effect on the overlying fascia and skin. I have been convinced in my cases that the movement of the tuberosity was distinctly under the deltoid and about as independent of it as in a normal shoulder.

Codman says that in the acute stages of a bursitis about 10 per cent. of painless motion is possible in the shoulder without calling into play the inflamed surfaces of the bursa. According to my observations, the floor of the bursa follows the greater tuberosity in its slightest movements, and that means that any movement of the arm, and therefore of the shoulder, brings the opposed inflamed surfaces into play. Küster makes similar statements, and goes so far as to say that even a push on the upper arm against the glenoid cavity does not give the slightest pain. I should say that if such a test did not elicit pain, there was no inflammation in the subdeltoid bursa, surely not acute enough to produce troublesome adhesions later. Again, Codman says that the local tenderness is sometimes definite enough to allow accurate mapping out of the bursa, especially in cases of inflammatory origin involving the whole bursa. It is difficult to conceive of an inflammation in a serous sac of the size of this bursa, intense enough to produce troublesome adhesions later, which does not involve the whole bursa. I doubt that such a bursitis could remain partial. I have seen, repeatedly, acute inflammation in other bursæ, as the prepatellar, that over the olecranon, and the "bunion" bursa, but there is rarely any doubt as to the diagnosis in them. Even if there were no redness or swelling, the acute tenderness would be so distinctly localized and so marked that no other condition would be suggested. I believe that the tenderness should be just as acute and as easily localized in a subdeltoid bursitis, especially when the arm is in the position of rest. The bursa, as already stated, is then almost entirely under the muscle and directly in front of the acromion. The tuberosity upon which the bursa lies

is almost subcutaneous, so that by pressure with the finger downward on the bursa against the bone, exquisite tenderness should be elicited and the limits of the bursa outlined almost exactly. The absence of tenderness should positively exclude bursitis. A push on the upper arm against the glenoid cavity would drive the upper end of the humerus against the under surface of the acromion, and, therefore, the inflamed surfaces against each other. Rather than not give the least pain, as Küster states, it should give acute pain, and the fact that it did not give pain in Küster's cases tends to show that the real trouble was elsewhere. The symptomatology of these cases in their various stages, as outlined by Codman and Küster, is essentially the same, and agrees with what I have observed in my own cases.

The etiology offered by both these writers is not satisfying, in my opinion. The relationship shown between cause and effect is not convincing. Codman suggests a variety of causes under the general headings of trauma, fixation of the arm and shoulder by dressings, and infections. Infections of this bursa are admitted to be very rare, and they will not be discussed here, since the cases under discussion are distinctly traumatic, or at least not pyogenic. Under trauma are suggested a direct blow from a fall, sudden muscular exertion, pressure as from a misapplied bandage, overuse as in a base-ball pitcher, and unaccustomed exertion without proper previous training. I believe that in a fall there is small chance for a direct blow on the bursa, which is on the top of the humerus, and with the arm at the side, is in front of the acromion. Indeed, I believe that a conscious person in falling practically never keeps his arm at the side of the body, but that he will from the instinct of self preservation unconsciously break the force of his fall by putting out the arm rigidly extended at the elbow and striking the ground with the hand. Such use of the limb accounts, I believe, for the great variety and frequency of injuries to the upper extremity and makes unlikely frequent striking on the shoulder. The falling of the arm to the side of the body before the patient realizes what has happened and the severe pain in the shoulder will account for the statement of the patient that he struck on his shoulder. Direct blows are not frequently productive of acute inflammation in the more exposed bursæ, and inflammation should, therefore, be much less common here. The function of the bursa is to provide for sudden muscular exertion and to obviate its untoward influence. It rarely produces inflammation in other bursæ. Again, misapplied bandages, overuse, and unaccustomed use are unlikely causes of inflammation here. Most bandages applied to the shoulder are used to immobilize the arm at the side of the body, and in my experience they usually tend to slide upward and rarely make firm pressure over the upper end of the humerus. Bandages about the elbow and knee are more likely to produce bursitis from

pressure, but very rarely do so. Nor do I believe that long fixation, as in the treatment of fractures, will cause a bursitis. Fractures of the upper end of the humerus or dislocations may injure the bursa, but rest alone can scarcely be regarded as a cause of inflammation in it. In my opinion neither the symptomatology nor the etiology as given by Codman and Küster localize the seat of the trouble in the subdeltoid busra.

I have seen in all 14 cases of these stiff and painful shoulders. They varied more or less from each other, but the differences were of degree rather than of kind. The scapulohumeral ankylosis, the pain particularly upon forced movement, and the impaired power of the muscles of the extremity, especially of the arm, were present in all. In all but 3 a clear history of trauma was obtained, and in 2 of these trauma could be excluded. In the other there was a vague history of muscular strains on several occasions, but I am now inclined to believe that it was not traumatic, but rheumatic. In 4 cases there had been a dislocation of the ordinary anterior variety in each. It seemed easy enough to account for the condition when it followed a dislocation, but in those in which there had been no dislocation the pathology did not apply. Yet I felt satisfied that it was essentially the same in all. The cadaver specimens in the department of Applied Anatomy of the University of Pennsylvania, through Dr. G. G. Davis' kindness, were always at my service, and I consulted them frequently. After reviewing the mechanism of the dislocation, with the aid of the dissected dislocation specimens and those in which the joint was unopened, it occurred to me that a sprain of the shoulder from forced abduction might explain those stiff and painful shoulders not due to dislocations. The difference between a sprain and a dislocation is often a narrow one. A sprain is the result of indirect violence which forces a movement of a joint beyond its physiological limits, with a stretching or tearing of the strained ligament. I believe that ligaments do not stretch much, but usually tear under these circumstances. There may even be a temporary dislocation with immediate reduction.

We hear very little of sprains of the shoulder, and yet when a force is applied to it sufficient to carry it beyond its physiological limits, something must give way. From my study of the joint specimens, I have satisfied myself that it is the capsule which makes the last stand for the protection of the integrity of the joint. In producing a dislocation of the shoulder on the cadaver by forced abduction, the first sensation of a giving way in the joint is synchronous with an audible tearing. On dissecting the specimen after the dislocation, usually nothing else will be found torn except the anterior and lower part of the capsule. The fact that the capsule tears extensively every time and usually alone proves that it is the structure which feels the first strain in overabduction of the

shoulder. Now, when we study the shoulder, we find that movement cannot be carried beyond the normal in adduction, the body being in the way. Therefore, the upper part of the capsule cannot easily be torn by such a movement. Movement of the arm forward and backward as in the pendulum movements, merely twists the capsule in its whole circumference, so that a tear is much less likely than if the strain were put on any one part of the capsule. To put the posterior portion of the capsule on a strain the arm must be carried forward and inward across the front of the chest, which again obstructs the movement. The portion of capsule most frequently and most violently exposed to strain by movement of the arm is the lower and anterior part, from forced abduction. From the position of rest at the side of the body, this is the least restricted movement of the arm, and when the force is applied to the hand with the elbow in extension, as in a fall on the hand, we have a very powerful leverage action at the shoulder.

The long axis of the glenoid cavity is directed from above downward and backward, so that the portion of the capsule usually regarded as anterior, that is, the portion anterior to the attachments of the long head of the biceps to the upper margin of the glenoid process and the long head of the triceps to the lower margin, is in reality the antero-inferior portion. What is probably not generally appreciated is that the axillary portion of the capsule is almost entirely anterior to the glenoid cavity as we determine its boundaries. When the arms are raised in abduction, we can see the whole axilla from in front, while it cannot be seen at all from behind. The effect of forced abduction, therefore, is to strain the axillary portion of the capsule. If the force is sufficient, this portion is torn more or less extensively. If greater force is applied, and particularly if a thrust is added, as in a fall on the hand, the humeral head is carried over the anterior glenoid margin and we have a dislocation. The freedom of movement in abduction, unhindered except by the axillary portion of the capsule, and the frequency with which it is forced beyond its physiological limits, account, I believe, for the overwhelming preponderance of anterior dislocations. Forced abduction is the accepted cause for most dislocations of the shoulder, and this cause can only produce an anterior dislocation. As soon as the patient assumes the upright position the arm falls to the side of the body and the humeral head rises to a position just under the coracoid process. Rarely the head may catch in the axillary tissues so that the arm cannot fall from gravity, when we have a *luxatio erecta*, which occurred in one of my patients who developed a scapulohumeral ankylosis, or the head may rise part way and catch in a somewhat higher position, when the arm falls only to about the horizontal position, and we have a *luxatio horizontalis*.

Undoubtedly in many cases, as the arm falls the head fails to

catch in front of the glenoid process, and a spontaneous reduction is the result. It has frequently been my experience in cadaver work to find that after the capsule has been felt to tear, considerable force was still necessary to effect the dislocation. Sometmes after the dislocation is produced still more forcible manipulation is necessary before the dislocated position can be maintained, when the arm is brought to the side of the body. The obvious inference from these facts is that many times in the living not enough force has been applied to produce a dislocation that will persist after the arm falls to the side of the body, and probably much more often the capsule is torn in various degrees short of that which is necessary for the occurrence of a dislocation.

Let us assume for the present that the forced abduction is the result of a fall. At the moment of impact the patient is so distracted that he is not capable of observing and afterward of recalling what was the actual position of the arm at the time. Most patients are not made unconscious from such an accident, and immediately afterward sit up or stand. In the meantime the arm may have been in various positions before it fell to the side of the body, and the patient is not impressed with the importance of any one of them. What he does know is that he fell and has pain in his shoulder. The simplest explanation to him is that he struck on the shoulder. A case seen with Dr. J. W. McConnell was very suggestive in this connection. The patient was descending a vertical ladder, when his feet slipped. The weight of his body compelled first one hand to lose its grip and then the other, and he fell to the ground. The patient accounted for his stiff and painful shoulder, which was accompanied by loss of power in the arm, by saying that he struck the shoulder on the ground. It was the shoulder on the side of the hand which was the last to lose its grip that became stiff and painful, and that was the shoulder probably exposed to the most severe abduction, as it was with that hand that he had the last chance to save himself from falling. The results of treatment, so far as they can, confirm the diagnosis of a contracted capsule. Dr. McConnell had had a fairly large experience with similar cases, and had hitherto treated them on a basis of a traumatic neuritis, with electricity, massage, and passive motion. In this case, in addition to the other measures, he employed forced abduction, to stretch a supposedly contracted capsule, and had the patient apply this exercise whenever possible, as by hanging from a horizontal bar or by any other means that presented itself. Recovery was very much more rapid than in any case he had previously treated.

A tear of the axillary portion of the capsule may occur in the absence of a fall or severe violence of any kind. I have seen a case in which there was one of these stiff and painful shoulders, of about eleven weeks duration, which was diagnosticated as a

circumflex neuritis, chiefly because the woman after careful questioning could not recall having sustained any injury to the shoulder. The *x*-rays showed a complete subcoracoid dislocation of the shoulder, which in my opinion implies an extensive tear of the capsule. She then recalled that about the time of the beginning of her trouble she had tried to move some heavy furniture, and had done something else of the kind, but she could not say which, if either, had started the disturbances in the shoulder. Another patient dislocated her shoulder while raising her arms above her head in the act of "stretching," when the rocking chair in which she was sitting tipped backward suddenly. There was considerable pain in the shoulder afterward, but not enough to prevent her from going to the theatre the same evening or to cause her to call her physician, although her husband was a dentist whose intelligence and solicitation would have led him to call a physician if there had been any suspicion of a dislocation. If the capsule will tear sufficiently to permit a complete dislocation without more evidence of it than developed in these cases, then it may be assumed that less severe tears from overabduction and muscular action are common and are not detected.

Codman cites, as a cause of subacromial bursitis, the vigorous friction produced between the bursal surfaces by a baseball pitcher in violently throwing a ball. May not the trouble which follows be due to a tear of the capsule? A dislocation of the shoulder has been produced by this action. The movement here is first into extreme abduction, from which position the hand and arm are brought downward and forward with much force, by the powerful adductors forming the folds of the axilla and having their insertions into the upper end of the humerus. With the axillary portion of the capsule under tension, the powerful pull of these muscles against it might readily tear it. A similar tear might be the result of getting off a street car with the hand gripping the hand rail and the body being dragged by the arm, if the patient lost his balance. I have already referred to a patient who probably received his injury from suddenly being compelled to support his whole weight on one hand with the arm in full abduction. It is unnecessary to go further in suggesting how in common accidents a tear of the capsule from forced abduction could occur.

Sprains in most joints are recognized easily, why not in the shoulder? Because the arm usually drops to the side of the body before the patient recovers from the excitement of the accident. The importance of the indirect violence which produced the forced abduction, is lost sight of, and the more obvious direct violence from the fall attracts attention. The seat of the lesion in the capsule is so deeply situated in the axilla that it cannot be localized by the symptoms which follow. The arm is kept at rest by the pain, that is, with the elbow at the side and the forearm across the front

of the chest. Abduction and external rotation pull upon the torn portion, adduction and internal rotation relax it. Since the nature of the lesion is not suspected by the attending physician, he advises rest in the most comfortable position, and too often it is kept in this position until the tear has healed and the capsule firmly contracted in its relaxed portion. The more severe the tear the greater the amount of inflammatory material formed about it and the more rigid the contraction. The blood and lymph from the torn vessels and the synovial fluid from the joint, freely opened in the dependent portion, extravasate around the muscles, the blood-vessels, and the nerves, and aggravate the rigidity of the joint. The nerves become involved in the inflammatory process which ensues, and later are bound down by the cicatricial tissue and adhesions. The pain is most marked in the early stages in the region of the lesion, but later may be transferred along the course of the imprisoned nerves. It is not material to account for the exact location of the transferred pain. I have seen it referred to the wrist. It is my belief that serious rupture of the nerves, even of the circumflex in dislocations, is comparatively rare, and that the prognosis with proper treatment is very good in the great majority of cases.

If the importance of the causal movement is not appreciated, it may be forgotten by the patient and a traumatic history may not be obtained, as in the case already referred to, in which a diagnosis of circumflex neuritis was made and a dislocation found later. A case ascribed to rheumatism may have originated in a forgotten injury, but it may be due to rheumatism. I have seen a case in which both shoulders were involved and rheumatism was partly at fault. This patient was a young lady who had been acting for several years as her father's secretary. About three weeks after the trouble began in her shoulders and in other joints, she fell down two steps, but did not observe that the accident was followed by any decided increase of the pain in the right shoulder. Yet it was this shoulder which gave her most trouble. Her physician, on account of the marked weakness in her arm and hand, and her inability to write, diagnosticated a writer's cramp. Upon consulting a second physician, he called it a neuritis of the arm. About six weeks after the fall, a third physician said that he discovered a dislocation of the shoulder, which he reduced without an anesthetic. Both the patient and her father are certain that there had existed, before the reduction, a depression below the acromion into which the fingers could be pushed. This symptom alone, in my opinion, justifies the diagnosis of a dislocation, particularly as the depression below the acromion disappeared after the reduction, which was followed by immediate and marked improvement in the shoulder and arm.

In a second case the condition could not have been due to trauma,

but was due to a non-traumatic inflammation of both shoulders. This second case was examined by a neurologist, who diagnosticated a chronic anterior poliomyelitis. The prompt improvement under massage and passive movements eliminated the spinal cord condition. If the arms are maintained in the position of rest during a prolonged attack of rheumatic inflammation, it is easily conceivable that the capsule should become more or less thickened and rigid, the axillary portion becoming shortened because relaxed. After the subsidence of the attack, when an attempt is made to abduct the arm and rotate it externally, the contracted axillary portion will offer resistance according to its degree of rigidity. The great majority of the cases, however, are distinctly traumatic.

Upon the basis of a torn capsule, I believe that all the various symptoms peculiar to these cases can be explained. The scapulohumeral ankylosis will vary widely, but is never complete, because there is always some remaining laxity in the affected portion of the capsule. If a severe tear of the capsule occurs in an old woman who has nothing else to do but nurse it, and particularly if she is very sensitive to pain, an aggravated case will result. One of the worst cases I have seen was in an old woman, who from a fall had sustained a fracture of the neck of the femur, which compelled her to lie in bed for many weeks. She had complained of pain about the shoulder after the accident, and some ecchymosis had appeared, but the *x*-rays did not reveal a fracture, and nothing was done for the shoulder except to keep it at rest. The limitation of movement in the shoulder and the atrophy of the surrounding muscles were very marked when I first saw the patient, about ten weeks after the acident. If the capsule tear is a slight one in a strong, active, and ambitious man, who persists in forcing the use of the arm at every opportunity, the return of function will be much more rapid, although even in such a case many weeks may be necessary before the normal range of motion is obtained. It is in the later stages of the latter type that the scapulohumeral ankylosis may be most difficult to detect, and for that reason the diagnosis may be very uncertain. The loss of power in the arm may be very marked, or there may be a very troublesome pain radiating down the arm. I have thought that the inclusion of the nerves in the old area of inflammation must be largely responsible for both. I have seen one case in which there was a slight scapulohumeral ankylosis, detected only by careful watching of the scapula and comparing its movement with the opposite side. Yet there was a marked weakness of the muscles on that side, although they seemed to be almost as well developed and to contract almost as well as in the normal arm. In another case, in which the ankylosis was marked and of long standing, there was considerable loss of power in the arm, but I had not paid particular attention to the condition of the hand. Under ether I forced the arm into

full abduction and fixed it there. He had not recovered from the anesthesia when I left him, and on the following day he expressed much satisfaction because he could, since he became conscious, perform all the normal movements of the hand. He said that before taking the anesthetic, the hand movements were much impaired and weak, but soon after recovering from the ether he found that they had all returned as if by magic. It would seem, therefore, that the limitation of movement in the shoulder *per se*, was responsible for some of the loss of power. On the other hand, almost the full power of the muscles may apparently return in time, though the limitation of movement persist. I have seen a patient with scapulohumeral ankylosis of about twenty-five or thirty years duration, so marked that the arm could be abducted only to a right angle with the body, and that with the associated movement of the scapula, yet there was only slight loss of power in all the muscles employed in producing the limited movements.

The following case is the best example in my experience, illustrating how a diagnosis of neuritis is made in some of these cases. I was visiting the patient as a friend, when he informed me that he had been under the care of his family physician for some time for a "neuritis" of the arm. The patient and his physician believed that the most likely cause was a habit of sleeping with his head resting on the arm. The pain was most marked at about the insertion of the deltoid, but radiated down the arm to the elbow and into the forearm. I was asked to examine the arm and did so, but I did not make a diagnosis. On another visit I found that he had tried various treatments, including "electrical treatment" and a patent medicine. The condition was still regarded as a "neuritis," and no one had ever suggested the possibility that anything might be wrong with his shoulder. Having become interested in these stiff and painful shoulders by this time, I tried the shoulder in this case and found a very marked limitation of abduction and external rotation and some slight grating on movement. I had not yet satisfied myself concerning the nature of these cases, and I thought that I was dealing with a case of osteoarthritis, and had his physician send him to a well-known orthopedic surgeon, who concluded that it was a case of osteoarthritis. Later the patient fell into the hands of an osteopath, who among other treatments carried out a vigorous series of forced exercises calculated to increase the limited movements, and after a prolonged period gave the patient a practically normal arm and shoulder. He did not have "neuritis," nor did he have osteoarthritis. He probably had had some time previous to the pain in his arm an attack of inflammation from rheumatism or an overlooked trauma in the shoulder, which had brought about a contraction of the axillary portion of the capsule, which in turn was lengthened again to the normal by the forced abduction and external rotation.

The most convincing evidence, in my experience, that these stiff and painful shoulders are due to a contracted capsule, is the fact that identically the same condition, so far as I can see, is present after the operation of contracting the axillary portion of the capsule for a recurrent dislocation of the shoulder. I have done this operation in eight cases, and I can see no essential difference between the two classes of cases, except in the results of the efforts to obtain movement. After the operation I can get movement in the shoulder more quickly and with less pain than in a case in which the capsule has recently been torn by accident. It may be that in the latter the extravasation of blood and synovial fluid among the axillary tissues produces a greater degree of inflammation and rigidity than follows the operative trauma. I had one experience in which I was positively convinced that the stiff and painful shoulder, in this case at least, was due to a contracted axillary portion of the capsule, because in that one the tearing sound produced by the leverage of the arm when it was forced into full abduction under ether, was accompanied immediately by a dislocation of the humeral head into the axilla. In my opinion, a traumatic dislocation of the shoulder implies an extensive tear of the capsule.

TREATMENT. While there seems to be a tendency to slow improvement in the function of the shoulder from long-continued efforts to use it even when untreated, I have no doubt that many cases remain seriously crippled through life. I know of one case in which the arm, after a dislocation of the shoulder about four years ago, is still seriously limited in the range and power of its movements. I have already referred to a case in which there is still marked limitation of movement, although the power is good and there is no pain twenty-five to thirty years after the original accident. A medical friend informed me that his grandfather died at a ripe old age, still carrying one of these stiff shoulders which was the result of an accident in early life. I believe, however, that with persistent treatment based upon the pathology which I have offered, practically all of them can be given normal, or nearly normal, function. In some there may be serious nerve lesions, but these are probably far from frequent. The majority of these patients will likely call for the physician's aid sometime after the original accident, when the limitation of movement and pain threaten to become permanent. If they are seen early and are very painful, the most important indication will be to provide rest of the shoulder by immobilization. During the early stages it may be necessary to immobilize it for a week or two, but during this period, at each change of the dressing, massage and passive movement within the painful limits is advisable.

The position in which the arm is to be immobilized is of importance. Küster applies a plaster cast with the arm at the side of the body for eight to fourteen days, and then begins careful passive movements, baths, and massage. Codman prefers to keep the

arm in abduction to a right angle or more. I regard this as a distinct advantage in reducing the later limitation of motion. I should prefer to vary the position in this stage according to the type of patient. If I were treating an ambitious young man who insisted upon attending to his business, I would dispense early with the fixed abduction, bind the arm at the side, and support the wrist in a sling from the neck. I would remove the dressing daily, and as soon as the pain would permit begin gentle massage and passive movements, gradually increasing the force until the length of the injured portion of the capsule and therefore the motion had been increased to the normal. If the patient were a highly nervous and sensitive woman, I would advise her to remain in bed, and would then adopt some measure for keeping the arm in full or nearly full abduction. This would permit healing of the injured portion of the capsule at nearly its normal length. If an obtuse angled splint is employed, this may be removed daily, when gentle massage and passive movements could be carried out. At the end of two weeks, or at most three, the arm may be lowered to the side of the body gradually, after which it can be brought back to the fully abducted position more easily than if it had been dressed at the side in the early stages. If the patient will not remain in bed, and, in the case of a man, if he is content to remain away from his business for a week or two, it becomes necessary to find a method of fixation of the arm in the abducted position that will permit him to walk about. This is not as simple a matter as at first it might seem. The position is an awkward one, exposes the patient to considerable discomfort, and the splint and bandage to such a strain that they tend to become disarranged. Monk's splint with Codman's modification is a particularly good one. In a case of subacromial dislocation in a boy upon which I operated, and in which I wished to maintain the fully abducted position for two weeks, I employed a light palster cast encircling the chest and the arm to but not including the elbow, and found it very satisfactory.

After the reduction of a dislocation of the shoulder we have the same problem to deal with, although the statistics of Schulz[4] show that we do not appreciate the fact. In these cases, however, the capsule has been so extensively torn that if we dress the arm in the fully abducted position we are in danger of permiting a recurrence and of the development of a recurrent dislocation. In Schulz's 54 dislocations of the shoulder, in not one was a recurrent dislocation developed. It would seem that the treatment was at fault in the opposite direction, that is, not enough force was employed in overcoming the cicatricial contraction of the torn axillary portion of the capsule in the early stages. At the end

[4] Deut. zeit. f. Chir., 1908, lx, 333.

of three weeks of rest of the arm at the side of the body, abduction with moderate force should be begun, and at the end of five or six weeks I believe that there will be little danger of producing a recurrence of the dislocation.

If the case comes under observation in the late stages, after the cicatricial tissue in and about the torn capsule is firmly contracted and very resistant, the effects of forced abduction may be so slight, and the return of motion so slow, that it becomes advisable to anesthetize the patient and to break the resistance completely at one sitting. The scapula should be immobilized with one hand, while with the other grasping the elbow the humerus is used as a lever to tear the shortened capsule. The tearing at the shoulder may be felt or even heard. Sometimes a tearing sensation is felt over the internal condyle at the elbow. Codman believes that this sensation at the shoulder is due to the giving way of adhesions in the subdeltoid and subcoracoid bursæ. The sensation at the elbow, he thinks, is due to the transmitted vibration along the coracobrachialis muscle to the centre of the humerus. I believe that the tearing at the shoulder is of the contracted axillary portion of capsule, and in one case, which has already been referred to, I was sure of it because immediately after the tearing sensation occurred I found that I had to deal with an axillary dislocation of the humeral head. I maintained nearly full abduction on a splint for about ten days, before letting the arm down to the side of the body. After about four months the patient had not had another dislocation and had nearly full motion at the shoulder. Nor do I believe that the sensation at the elbow is a transmitted one, because a few days after the forcible manipulations in one case, in which I felt the tearing sensation over the internal condyle, there appeared a slight but distinct area of ecchymosis over the internal condyle, showing that something had actually torn there. I prefer to believe that the slight injury at the elbow was due to the pull on the triceps, the long head of which is caught in the contracted cicatricial portion of the capsule.

After the capsule has been torn and full abduction produced, provision must be made for maintaining that position, just as in some cases in the acute stage following the original accident. After using force to break the resistance, Küster dresses the arm for a time at the side of the body, and he speaks of the necessity of frequent repetition of the "breaking of adhesions." He says that only in very old cases should the hope of complete success be abandoned. I have had four cases in which I used force under the influence of an anesthetic, and in none was it necessary to repeat it. In one, a young, vigorous man, there was perfect function in three months, and in another, also a young man, there was almost full motion in the shoulder in six weeks, when I lost sight of him. In the two others, one a man and the other a woman, both

about sixty-five years of age, there was nearly full function in four months. One is still under treatment and the other had nearly full function when she disappeared.

The principle is the same as when the tendo-Achilles is divided for talipes equinus. As the gap in the tendon is bridged across, so the gap in the torn capsule, which is probably not more than a half inch wide, is filled in with new cicatricial capsule in a short time. After two weeks rest in the abducted position, the arm is gradually lowered to the side of the chest. Massage and passive motion are then depended on to bring about a return of function in the joint and atrophied muscles and a stretching of the adhesions and absorption of the inflammatory material about the nerves and vessels in the axilla.

In those cases in which the scapulohumeral limitation of movement is slight and the pain referred down the arm marked, the question arises as to whether forcible abduction is advisable to tear the slightly shortened capsule. In the one case of this kind in which I tore the capsule, the patient as soon as he recovered from the nitrous oxide anesthesia, said that he had felt the tearing at the shoulder, and expressed the belief that the real cause of his trouble had been removed. After a few days rest in bed, with the arm in full abduction on a splint, I allowed him to get out of bed with the arm at the side, but only on the promise that he would permit full abduction at least once daily. The marked lack of power and the severe pain in the arm, particularly on efforts to abduct it, which had persisted for eight months, during which time he could not follow his usual occupation as a machinist, rapidly improved, so that in six weeks after the forcible manipulations he was able to return to work at his trade. This is the best kind of evidence that the slightly contracted capsule, was chiefly responsible for the "paralysis" and the pain which had been ascribed to a "neuritis."

Conclusions: A periarthritis from tears of the axillary portion of the shoulder capsule, due to forced abduction, offers the best explanation of the stiff and painful shoulders, with loss of power in the arm, variously diagnosticated as fibrous ankylosis, neuritis, paralysis of the deltoid, traumatic arthritis, etc.

The most characteristic feature is a scapulohumeral limitation of movement, sometimes slight, often marked, but never complete. The associated loss of power and atrophy are due in part to disuse, but probably in most part to the perineuritis, neuritis, and resulting adhesions and compression of some or all of the brachial nerves in the axilla, adjacent to the wounded joint.

Subacromial, or subdeltoid bursitis does not explain satisfactorily the symptomatology in these cases, nor is it accounted for by the etiology usually suggested. The audible and palpable tearing which accompanies the breaking up of the limited abduction and

external rotation, in chronic cases, by the leverage of the arm, under an anesthetic, is produced not by the tearing of fibrous adhesions in the bursa, but of the axillary portion of the capsule shortened by cicatricial contraction in its relaxed condition.

This bursa is circumscribed to the upper surface of the greater tuberosity of the humerus and the adjacent small portions of the rotators inserting into it. When the bursa is inflamed the diagnosis should be easily made by the acute tenderness localized to the upper surface of the humerus, directly in front of the acromion, when the arm is in the position of rest, that is, adduction and internal rotation, which it practically always occupies.

The capsule lesion is typified by that which occurs in an anterior dislocation of the shoulder, the frequency of which is nearly as great as that of all other dislocations of the shoulder combined. Those cases of stiff and painful shoulder in which there is no history of dislocation are explained, in the first place, by the spontaneous reduction of many dislocations as the arm falls from its abducted position to the side of the body, so that they are not recognized as such; and in the second place by the much greater frequency of milder but similar tears (sprains) from forced abduction, which are not sufficiently extensive to permit the occurrence of a dislocation.

Sprains are rarely recognized in this joint, because they are peculiarly obscure as to their etiology and symptomatology. At the moment of the forced abduction the patient is excited and does not appreciate the relation between this movement and the pain it produces, the capsule being poorly supplied with nerves and the pain of the moment probably slight. The arm immediately drops to the side into the position of most complete relaxation of the torn portion of capsule, and is kept there afterward because of the pain produced by abduction and external rotation which drag on the seat of injury. The lesion is deeply seated and localized with difficulty, and the disturbances which follow are misinterpreted.

The most rational method of treatment is that which aims at increasing the length of the contracted tissues to the normal, favors the absorption of inflammatory material, and increases the power of the weakened and atrophied muscles.

THE INTERRELATION OF THE ORGANS OF INTERNAL SECRETION.[1]

II. THE PITUITARY

By R. G. Hoskins, Ph.D.,
PROFESSOR OF PHYSIOLOGY IN THE STARLING-OHIO MEDICAL COLLEGE, COLUMBUS

(From the Laboratory of Physiology of the Harvard Medical School, Boston.)

The Pituitary. It has seemed best to discuss the pituitary as a single organ, since it is very generally so treated in the literature; but this is on the score of convenience merely since in its two lobes we are dealing with entities of distinct origin and different functions. This structure will be considered in relation to the thyroid, the reproductive organs, the adrenals, and the pancreas.

Pituitary-thyroid Hyperpituitism. The effect of experimental hyperpituitism upon the thyroid has been as yet but little studied—largely, probably on account of the difficulty of obtaining pituitary material. That a condition parallel to true hyperactivity of the normal gland can be secured by the injection of extracts or by feeding gland substance is by no means so sure as in the case of the thyroid. Hallion and Alquier[2] subjected five rabbits to prolonged ingestion of extracts of the pituitaries of cattle, using the whole gland. At autopsy the thyroids were found to contain less than the usual amount of colloid, and the cells were somewhat more nearly columnar than normal. Rénon and Delille[3] obtained the same results, using intraperitoneal injections of extracts of the gland. They found that the use of the posterior lobe alone had effects similar to the use of the whole gland. This result is incidentally in harmony with the usual results reported by other investigators, who have uniformly found extracts of the anterior lobe without physiological effect. Both sets of experiments indicate that the active substance of the pituitary has a slightly stimulating effect on the thyroid. Lucien and Parisot,[4] however, have repeated the experiments of Rénon and Delille and obtained somewhat different results. They noted a hypertrophy in the thyroids of from 10 to 40 per cent., with an increased amount of colloid—an appearance "hardly indicating increased activity, but rather resembling a simple goitre." Sandri[5] found in guinea-pigs that feeding or injecting pituitary extracts caused in other organs no demonstrable effect whatever. Similar results have been obtained by the writer in case of nineteen young guinea-pigs. The evidence, therefore, on the whole, is inconclusive.

[1] Concluded from page 385.
[2] Comp. rend. Soc. de biol., 1908, lxv, 5. [3] Ibid., lxv, 499. [4] Ibid., 1909, lxvi, 675.
[5] Arch. ital. de biol., 1909, li, 337.

Hypopituitism. The little existing evidence as to the effects of deficiency of pituitary secretion upon the thyroid, is positive and clear cut. Cushing,[6] after an extensive study of the results of hypophysectomy in young dogs, states explicitely that the operation causes acute hypertrophy of the thyroid. An instructive study has been made by Exner,[7] of two of Hochnegg's surgical cases, that were essentially experiments bearing directly upon this point. In both instances the pituitary had been extirpated for the relief of akromegaly, and later there was found, among other results, an undoubted hypertrophy of the thyroids.

These results bear a suggestive similarity to the effect of thyroidectomy upon the pituitary and justify an extension of the theory of vicarious activity to include both glands. The theory implies that the glands are more or less synergic. The hypothesis is further supported by the observations of Soli[8] that after castration in all but 5 of 25 cases, hypertrophy of the pituitary occurred; in these 5, the *thyroids* were enlarged. Taken altogether, the evidence supports a theory that the two glands are synergic and either can to some extent, in case of need, function vicariously for the other.

Pituitary; Gonads. Clinical observers have noted that disturbances of pituitary function—either by tumors in the gland itself, or by pressure of brain tumors near it—are frequently associated with sexual anomalies.[9] [10] Cessation of menstruation in the female and impotence in the male are recognized initial symptoms of akromegaly,[11] [12] and the same effects are noted when neoplasms exert pressure upon the hypophysis.[13] The two previously mentioned cases of akromegaly described by Exner are especially significant in this connection. The onset of the disease in each instance was marked by the development of amenorrhœa. The restoration of menstruation after the removal of the tumors indicates a specific causal relationship of the pituitary conditions. Thumin[14] has reported the case of a young woman whose sexual functions became erratic with the development of a pituitary tumor, and whose ovaries atrophied as the disease progressed. Other cases of adults of both sexes, in whom atrophy or aplasia of the gonads (infantilism) has been associated with pituitary tumors, have been described by Cushing,[15] Schuller,[16] Kon, v. Eiselsberg, and

[6] Jour. Amer. Med. Assn., 1909, liii, 249.
[7] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1909, xx, 620.
[8] Arch. ital. de biol., 1910, lii, 353.
[9] Kon. Beitr. z. path. Anat., 1908, xliv, 233.
[10] Church. Jour. Amer. Med. Assn., 1909, liii, 97.
[11] Cagnetto. Virch. Arch., 1908, clxxxvii, 197.
[12] Kon. Beitr. z. path. Anat., 1908, xliv, 266.
[13] Axenfeld. Neurol. Centralbl., 1908, xxvii, 608.
[14] Berl. klin. Wochensch., 1909, xlvi, 631.
[15] Amer. Jour. Nerv. and Ment. Dis., 1906, xxxiii, 704.
[16] Neurol. Centralbl., 1907, xxvi, 965.

v. Frankl-Hochwart,[17] Rénon, Delille, and Monier-Vinard,[18] and by Schloffer.[19] A particularly instructive case has been reported by v. Eisel berg;[20] a young man, aged twenty years, developed a typical case of *degeneratio adiposogenitalis*, with a tumor of the pituitary, and infantile sex organs. The tumor was successfully removed, and a year later, marked genital development had occurred.

Clinical evidence of this nature supports rather convincingly a conclusion that there is some sort of coördination between the activities of the hypophysis and of the gonads. The actual significance of the data, however, is obscured by the uncertainty that prevails as to the etiology of akromegaly. The disease is usually ascribed to hyperplasia of the pituitary, that is, to *hyperpituitism*, but the effect upon the gonads is often the same as that of obliterative tumors, that is, of *hypopituitism*.

Hyperpituitism. As mentioned before, few experimental observations upon the effects of hyperpituitism have been reported. None in which the gonads were considered are known to the writer, except those previously discussed by Hallion and Alquier, Rénon and Delille, and Sandri. As regards the sex glands, negative results were reported in each case.

Hypopituitism. The evidence as to hypopituitism is likewise meagre. Although many partial and complete hypophysectomies have been made, but little attention apparently has been paid to the effects upon other organs of internal secretion. Cushing, however, has noted that after extirpation of a part of the anterior lobe, the gonads often atrophy. It is interesting to note that a tendency to obesity, such as is observed after castration, also occurs. This evidence, together with the observed effect of obliterative tumors in the hypophysis region, indicates that the pituitary normally supplies a secretion that stimulates the sex glands to activity. More definite experimental evidence is needed, however, before a final conclusion can be reached.

Pituitary; Adrenals. The observations regarding a relationship between the pituitary and the adrenals are few. Hallion and Alquier have noted hyperplasia of the adrenal cortex after prolonged feeding of pituitary extract. After intraperitoneal injection of a similar extract, Rénon and Delille have obtained the same result. In both cases the posterior lobe alone was effective. No other data upon this relationship have been found in the literature. Any valid conclusion, therefore, in regard to the matter is obviously impossible.

Pituitary; Pancreas. Whether there is any direct relationship between the pituitary and the pancreas is doubtful. Glycosuria

[17] Wien. klin. Wochensch., 1908, xxi, 1115.
[18] Bull. et Mem. Soc. Med. de hôp. de Par., 1909, xxvi, 204.
[19] Wien. klin. Wochensch., 1907, xx, 621.
[20] Neurol. Centralbl., 1907, xxvi, 994.

frequently occurs in akromegaly. Sternberg[21] regards this as due to changes in the pancreas. Benda,[22] however, thinks that there is no constant change in the pancreas in akromegaly, even in diabetic cases.

The evidence as a whole, indicates a mutual relation between the thyroid and the pituitary such that deficiency of the one leads to increased activity of the other. This is due to the vicarious assumption by the one, of the depressed function of the other. A tentative conclusion that the pituitary exercises a normal stimulating effect upon the sex glands is justified. The meagre data available indicate that the adrenals are stimulated by pituitary secretion, but give little weight to the conclusion. Whether the pituitary has any direct relation with the pancreas is questionable.

THE ADRENALS. The so-called "adrenal gland" consists of two parts, the cortex and the medulla, which are very probably physiologically independent structures. The only known active substance that has been demonstrated in the adrenals is produced entirely by the medulla. The two parts are of different embryonic origin, and in some of the lower fishes, they remain distinct throughout life. A separate consideration of the two parts would be desirable, therefore, in this work, but this would not be feasible because in the literature a distinction has not been consistently observed.

Adrenals; Gonads. A theory that the adrenals are related to the sex function was proposed by Meckel,[23] as early as 1806. It was based upon the following grounds: (1) In certain aborted fœtuses he had noted that both the adrenals and the gonads were lacking; (2) in animals in which sexuality is marked, such as the guinea-pig, the adrenals are notably large; (3) in birds and amphibia the gonads and adrenals are closely associated in position, and (4) he had noted adrenal degeneration in several cases of diseases of the genitalia. Meckel's evidence has been controverted by various writers, notably by Nagle,[24] but the idea has persisted and at the present time there exists considerable evidence in its favor. This is partly clinical and partly experimental.

In cases of hermaphroditism, marked hypertrophy of the adrenals is sometimes observed. Instances of this association of conditions have been reported in detail by Creechio[25] and by Marchand.[26] v. Neugebauer[27] in an extensive review of the literature of hermaphroditism published in 1908, was able to find record of 13 cases in which this association was mentioned. As evidence these few instances have no great weight, but they are suggestive.

[21] "Akromegaly," Nothnagel's Handbuch d. spec. Path. u. Ther., vol. vii, Band 2.
[22] Cited by Dock; Osler's Modern Medicine, 1909, vi, 468.
[23] Cited by Nagle.
[24] Müller's Arch., 1836, p. 365.
[25] Wien. med. Presse, 1866, p. 763. Cited by Bullock and Sequiera.
[26] Festschrift f. R. Virchow, i, 554.
[27] Hermaphroditismus beim Menchen., Leipsic, 1908, p. 688.

Bullock and Sequiera[28] have been able to find in the clinical literature 12 cases of children showing sexual precosity, who at autopsy, were found to have enlarged adrenals; 10 of these were females, from two to eleven years of age, and 2 were males, aged five and fifteen years respectively. In view of the fact that comparatively a small proportion of such cases come to autopsy at a time when the condition is recognizable, these findings are of some weight as indicating adrenal activity as a condition of sexual development.

Various other instances of associated sex and adrenal anomalies have been recorded. Otto[29] noted in a patient a simultaneous hypertrophy of the gonads and the adrenals. Wiesel[30] and Karakascheff[31] have each reported an instance of adrenal atrophy accompanied by sex depression, and Bullock and Sequiera mention 3 others. Borz[32] and Thumin[33] have recently described 2 cases of young women who had been sexually normal up to the age of sixteen years and in each of whom then, menstruation ceased; the voice became coarse, and an extensive growth of hair upon the body occurred. At autopsy both were found to have markedly enlarged adrenals. In Thumin's case, the ovaries were somewhat atrophic.

The clinical literature taken altogether indicates that there is a correlation between the adrenals and the gonads. It further suggests, too, a theory that the adrenals furnish a stimulus to the gonads. Such a theory, however, is susceptible to the general objection that associated conditions in the two organs may be effects of some common influence, and neither the cause of the other.

The truth of the theory has been tested but little by experimentation. It has been noted by Bossi[34] that goats can go through pregnancy and give birth to normal young after the removal of one adrenal. Hultgren and Anderson[35] have found the same to be true of the guinea-pig. The writer has noted, however, that f om a given number of guinea-pigs so treated, even though they appear perfectly healthy, the number of offspring secured in the course of a year is notably below normal. Landau[36] states that adrenal extirpation is without demonstrable effect upon the ovaries of adult rabbits. Since bilateral adrenal extirpation is rapidly fatal, however, and unilateral extirpation is notably ineffective

[28] Trans. Path. Soc., London, 1905, lv, 189.
[29] Pathol. Anat. Beobachtungen, p. 139. Cited by Bullock and Sequiera.
[30] Virch. Arch., 1904, clxxvi, 103.
[31] Beitr. z. path. Anat., 1904, xxxvi, 401.
[32] Arch. f. Gyn., 1909, lxxxviii, 445.
[33] Berl. klin. Wochensch., 1909, xlvi (1), 103.
[34] Arch. f Gyn., 1907, lxxxiii, 505.
[35] Skand. Arch. f. Physiol., 1899, ix, 73.
[36] Experimentelle Nebennieren-studien, Dorpat, 1908.

negative results are of slight significance, and scarcely modify the conclusion reached from a study of the clinical literature.

Adrenals; Thymus. The relation of the adrenals to the thymus has apparently received little attention, and there is some likelihood that the clinical evidence is defective simply for this reason. In 1902, Pansini and Bonenati described a case of Addison's disease in which in addition to the characteristic adrenal degeneration there was a marked hypertrophy of the thymus. In 1904, Wiese described a second case. In his report he discussed at some length the association of adrenal hypoplasia and thymus hypertrophy, and claimed priority for the discovery that such an association is common in cases of *status lymphaticus*. In view of this asserted relationship, Hedinger,[37] in 1907, made a study of all the material from cases of Addison's disease available in the pathological institutes of Berne and Basel, and found in a majority of the cases a recognizable condition of *status lymphaticus*. Other cases of this association have since been reported by Hart,[38] Pappenheimer and Kahn.[39] The clinical data are consistent so far as they go, but further observations are needed.

Very little experimental work upon the subject has been done. Boinet[40] at the autopsies of rats that had survived for a considerable length of time the extirpation of both adrenals found that 11 of 50 individuals showed thymus hypertrophy. Auld,[41] in 1899, in an investigation of "compensatory hypertrophy" found in each of four cats upon which he had performed unilateral adrenal extirpation a "very great hypertrophy" of the thymus. Other investigators who have performed epinephrectomies seem not to have paid attention to the condition of the thymus. The possible results in the thymus after this operation may have been overlooked because the animals either die within a short time, or if they survive long, become more or less cachectic. In the first condition, time would not have been allowed for hypertrophy to occur, and in the second, any tendency to hyperplasia would be masked by the marked tendency of the thymus to atrophy in case of deficient nutrition.[42]

On the whole, it appears that adrenal deficiency is frequently associated with hypertrophy of the thymus, and so far as the evidence bears upon the point, that is, in Addison's disease, and in experimental adrenal deficiency, that the condition in the adrenals is primary to that in the thymus. More evidence is needed, however, before any final conclusion can be reached.

[37] Verhandl. d. deutsch. path. Gesellsch., 1907, xi, 29.
[38] Wien. klin. Wochensch., 1908, xxi, 1119.
[39] Virch. Arch., 1910 (June).
[40] Comp. rend. soc. de biol., 1895, xlvii, 163.
[41] Brit. Med. Jour., 1899, p. 1327.
[42] Jonseri, Arch. f. mikr. Anat., 1909, lxxiii, 390.

Adrenals; Pituitary. The observations as to a relationship between the pituitary and the adrenals have been few. Boinet, in experiments previously mentioned, found pituitary hypertrophy following epinephrectomy in 4 only of 50 cases. Alquier observed also, in a dog, slight evidence of hypertrophy after the same operation. A similar effect in the guinea-pig, dog, and cat, has been noted by Marenghi.[43] Landau has found that in the adult rabbit adrenal extirpation is entirely without effect upon the hypophysis. At present, therefore, there is little evidence of any relationship of the adrenals to the pituitary.

Adrenals; Thyroid. Whether a demonstrable result in the thyroid follows adrenal extirpation is questionable. Boinet found hypertrophy of the thyroids in 12 of 50 cases. Landau, however, who has investigated the matter at some length, states that in his experience, adrenal extirpation has upon the thyroids no effect whatever. Parhon and Goldstein[44] noted in three dogs an augmentation of colloid in the thyroids after a short course of treatment with adrenalin. No definite conclusion in regard to this relationship is yet possible.

Adrenals; Pancreas. Previous mention has been made of Eppinger, Falta, and Rudinger's hypothesis that the chromaffin system and the pancreas are mutually antagonistic. An adequate discussion of the theory would necessitate a review of a long series of researches such as the scope of the present work scarcely permits. Their conclusions as regards the pancreas are based upon the fact noted by Blum, Zülzer and others that the injection of adrenalin causes glycosuria. The theory has the weakness inherent in our ignorance of many of the details of carbohydrate metabolism. It is supported by the observations of Rudinger, Falta, Eppinger, Pollak, and Porges[45] that in Addison's disease the dextrose limit is high. A final evaluation of the theory, however, must await the accumulation of more evidence.

In summary it appears that the theory of an association between the activities of the adrenals and the gonads is well supported, and there is some reason to believe that the former glands may stimulate the latter. Adrenal hypoplasia and thymus hyperplasia are frequently associated; probably the former condition stands in causal relationship to the latter. There is little evidence of a relationship of the adrenals to the pituitary. The theory that the adrenals stimulate the thyroids has some evidence in its favor but more data are needed; the same is true of the hypothesis that the adrenals inhibit the pancreas.

THE GONADS. While it is probable that the testes and ovaries, considered as organs of internal secretion, have little in common, it will be more convenient to consider them together.

[43] Lo Sperim., 1903, lvii. Cited by Alquier, p. 494.
[44] Rev. neurol., 1909, xvii, 1143.
[45] Zeit. f. klin. Med., 1910, lxx, 243.

Gonads; Pituitary; Hypergonadism.[46] No evidence has been found of any effect of activity of the male sex organs upon the pituitary. In the female, pregnancy has been observed to cause an increased activity of this gland. Launois and Mulon,[47] Morand, and Guerrini,[48] and Laignel-Lavastine have reached that conclusion from cytological studies. The matter has recently been determined conclusively by Erdheim and Stumme,[49] who have found from a careful comparison of the weights and cytological condition of the pituitaries from 85 pregnant women with 13 from nulliparæ that both pituitary hypertrophy and increased cellular activity accompany pregnancy. Whether this effect, however, is due to sexual activity *per se* is open to question. The increased activity may be simply a reaction to the changed metabolic conditions that undoubtedly occur during pregnancy. Laignel-Lavastine states that hyperemia and hypertrophy of the pituitary can be demonstrated during menstruation, but the assertion lacks corroborative evidence. Rénon and Delille[50] have reported that ovarian extract "moderates the pituitary" but their evidence is not convincing. No definite conclusion, therefore, can as yet be reached as to whether or not hyperactivity of the sex glands has any effect upon the pituitary.

Hypogonadism. The effects of castration upon the pituitary have been studied by several investigators. Cecca[51] has reported entirely negative results in both sexes; since, however, the details of his research are not given, a critical consideration of his work is not possible. Fichera[52] has studied the matter in 65 animals—cocks, 50; buffalo, 5; cattle, 5; guinea-pigs, 2; and rabbits 3 cases—and has found that castration in both sexes is followed by an undoubted hypertrophy of the anterior lobe of the pituitary, with a hyperplasia of the eosinophile cells. In three capons he found that injections of testicular extracts caused a rapid disappearance of the eosinophilic substance. Fischera's results seem well established and have been generally accepted as valid. His findings have been confirmed by Tandler and Gross,[53] by Soli, and by Schutz,[54] on animals and somewhat doubtfully by Kon in a study of the pituitaries of 7 women, and of 1 man, after surgical castration. The effects of this operation seem to be confined to the anterior lobe. These observations suggest that the pituitary may normally be held in check by secretions of the gonads, and

[46] "Hyper-" and "hypogonadism" are proposed as terms to indicate conditions due to excessive and depressed secretory activity, respectively, of the gonads considered as organs of internal secretion.

[47] Arch. de gyn. et l'obst., 1904, p. 1.

[48] Zeit. f. allg. Path. u. path. Anat., 1905, xvi, 177.

[49] Beitr. z. path. Anat., 1909, xlvi, 1.

[50] Comp. rend. soc. de biol., 1909, lxvi, 89.

[51] Presse Méd., 1904, xii, 341.

[52] Arch. ital. de biol., 1905, xliii, 403.

[53] Wien. klin. Woch., 1908, xxi, 280.

[54] Cited by Cushing; Amer. Jour. Med. Sci., 1910, cxxxix, 478.

that when this inhibition is removed, the pituitary manifests increased activity, leading to altered metabolisms and thus to an overgrowth of different parts of the body, such as occurs both in akromegaly, and after castration.

Gonads; Thymus. The evidence of a relation between the gonads and the thymus is not extensive, but is entirely concordant. That the thymus persists until puberty, when the sex glands undergo a physiological hypertrophy, has long been known. It would be *a priori* likely, therefore, that castration, would tend to prolong the persistence of the thymus. The facts bear out the supposition. Calzolari[55] apparently was the first to investigate the matter experimentally. In six castrated rabbits he found that the thymus invariably attained greater weight and persisted longer than in normal animals. Henderson[56] investigated the matter in 114 cattle that were being slaughtered for beef. They had, of course, been castrated while young. They were found generally to have persistent thymuses. The same fact was noted by Henderson in guinea-pigs and rabbits. It was noted, also, that in cattle of both sexes, that had exercised the reproductive function, the normal thymus atrophy was accelerated. Godall,[57] in a histological study of the effects of castration in the thymus of the guinea-pig, noted that both the lymphoid tissue and the corpuscles of Hassal share in the delayed atrophy. Soli in 10 rabbits and 15 capons has noted a similar thymus persistence after castration, and Tandler and Gross have found the same effect in roebucks, dogs, and goats. These writers state also, that persons with hypoplastic gonads retain their thymuses longer than normal. It can, therefore, be definitely asserted that the gonads exert a depressing effect upon the thymus.

Gonads; Adrenals. The effect of conditions in the gonads upon the adrenals has not been studied to any great extent. Guieysse[58] and Marrassini[59] have noted that in guinea-pigs the adrenals enlarge during pregnancy, but as pointed out previously, the interpretation of this condition as primarily a sex phenomenon is questionable. Cecca, Marrassini, and Tehodossief[60] have reported that hypertrophy occurs in the adrenal cortex after castration just as it occurs in the pituitary after the same operation. These observations have been confirmed by Soli. He has noted further that the hypertrophy is succeeded by an atrophy. This paucity of data, however, permits no final deduction as to the effects of conditions in the gonads upon the adrenals.

Gonads; Thyroid. But little is known of the effects of the gonads upon the thyroid. So far as has been discovered in the present

[55] Arch. ital. de biol., 1898, xxx, 71.
[56] Jour. Physiol., 1904, xxxi, 222.
[57] Jour. Physiol., 1905, xxxii, 191.
[58] Comp. rend. soc. de biol., 1899, xlix, 898.
[59] Arch. ital. de biol., 1906, xlvi, 73.
[60] Russky Vratsch., 1906, No. 5. Cited by Borz.

investigation the effects of testicular extracts upon this gland have never been studied. Ovarian extract injected intraperitoneally has been observed by Rénon and Delille to cause congestion or even hemorrhage in the thyroid; such an observation, however, is probably of slight significance as indicating any definite relation between the two glands. The thyroid often hypertrophies during menstruation and pregnancy, and this is sometimes interpreted as indicating a relation between the ovaries and the thyroid. Most observers have failed to note any effect of castration upon the thyroid, but Cecca and Delille, have noted in both sexes a hypertrophy. Soli observed no effect upon the thyroid of this operation in cocks, but in rabbits for the first three months there was a slight augmentation, followed later by a depression of the thyroid weights. The evidence altogether is too meagre in quantity, and conflicting in tenor to permit any conclusion as to a possible effect of the gonads upon the thyroid.

It appears that hypogonadism leads to hypertrophy of the pituitary possibly by removing a normal check upon it; activity of the sex glands seems to lead to depression of the thymus. A few observations indicate that the adrenal cortex hypertrophies after castration. The evidence as to the effects of activities of the sex glands upon the thyroid is meagre and not concordant.

The Thymus. Despite a great deal of work upon the subject, little is known of the function of the thymus, and of the data available few observations bear upon the relation of the organ to other glands. Previous mention has been made of the hypertrophy of the thymus that occurs in cases of Addison's and of Graves' diseases but the significance of the condition is unknown.

Thymus; Gonads. Paton[61] has reported that removal of the thymus in young guinea-pigs causes a more rapid growth of the testes than normal. Soli, however, has obtained in cocks and rabbits exactly the opposite effect. Whether the thymus, therefore, has any influence upon the sex glands remains an open question.

Thymus; Thyroids. Aside from a report by Lucien and Parisot[62] that a series of rabbits killed at varying periods after thymectomy had in every case smaller thyroids than the controls, there is no evidence known to the writer of a relation of the thymus to the thyroid. Soli after a series of 34 thymectomies found no demonstrable effect in the thyroids. In some cases he observed a slight but probably negligible augmentation of the weights of the pituitaries, and of the adrenals.

The Pancreas. Previous mention has been made of Falta's theory of the antagonism between the pancreas and the thyroids There is little direct evidence that the pancreas does depress thyroid activity. Licini[63] has noted in dogs, however, a pro-

[61] Jour. Phys., 1904, xxxii, 28.
[62] Comp. rend. soc. de biol., 1909, lxvi, 406.
[63] Deutsch. Zeit. f. Chir., 1909, ci., 522.

gressive hypertrophy of the thyroids with an increase in the colloid content after pancreas extirpation. The histological appearance of the thyroids in his opinion indicated an increased functional activity.

THE PARATHYROIDS. There is but little known of the relationships between the parathyroids and other endosecretory organs. Marinesco and Parhon[64] have noted after thyreoparathyroidectomy a marked increase in the fat-like material in the cells of the adrenal cortex. This change they at first ascribed to the removal of the thyroid, but after a repetition of their experiments, concluded that it was caused mostly or wholly, by the loss of parathyroid tissue. Caro and others have postulated an antagonism between the parathyroids and the thyroids, adrenals, and pituitary, on the grounds that the parathyroids depress the irritability of the nervous system, carbohydrate metabolism, calcium, and magnesium metabolism, and blood pressure. There is, however, little or no direct evidence on the point.

THE PINEAL BODY. There is some slight evidence that the pineal body may have an influence on the development of the gonads. Raymond and Claude[65] have recently reported in detail one instance and cited a few others of pineal tumors associated with sexual precocity. Such instances are too rare, however, to have any great significance.

In this work little mention has been made of the possible mechanisms by which the various effects described have been produced. Very suggestive is the work of Falta, Kostlivy, Caro, and others, which indicates that many of the symptoms of endosecretory disturbances are due to stimulation of the sympathetic and general autonomic nervous systems—sometimes acting concordantly, sometimes antagonistically. Other effects may be reactions to endotoxins due to perverted metabolisms. Others are probably due to direct hormone stimulation of various organs. Before the mechanisms of the various interactions can be fully understood, a much greater number of definite data must be secured.

The writer is aware that in the attempt to collect the evidence from such widely scattered sources, some significant observations may have been overlooked. He ventures to hope, however, that not enough has been missed to alter substantially the conclusions reached.

It is a sincere pleasure to acknowledge many obligations to Professor Walter B. Cannon for his helpful criticisms of this work.

[64] Roumanie Med., 1908, Nos. 10 and 11, 19 and 20.
[65] Bull. acad. med., 1910, lxxiv, 261.

THE SUDDEN ONSET OF PARALYSIS IN POTT'S DISEASE WITHOUT DEFORMITY OF THE VERTEBRÆ.

By Williams B. Cadwalader, M.D.,
PATHOLOGIST TO THE ORTHOPÆDIC HOSPITAL AND INFIRMARY FOR NERVOUS DISEASES; ASSISTANT INSTRUCTOR IN CLINICAL NEUROLOGY AND NEUROPATHOLOGY AT THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

(From the Laboratory of Neuropathology of the University of Pennsylvania.)

Compression of the spinal cord causing paralysis may be due to various morbid processes, but here I shall refer only to compression following tuberculous caries of the vertebræ or Pott's disease. Although both the clinical and pathological manifestations of this disease have been carefully studied, there are still many disputed points in regard to the exact means by which interruption of the functions of the spinal cord are brought about, so for this reason, and on account of some very unusual features the following cases seemed worthy of careful study. I wish particularly to express my thanks to Dr. Spiller, Dr. Mills, and Dr. Frazier who have kindly furnished me with the material upon which this investigation is based.

Case I.—A colored male, aged thirty-eight years, was admitted to the Philadelphia Hospital in the service of Dr. C. K. Mills, November 7, 1904, complaining of paraplegia. His family history revealed nothing of importance. He denied syphilis. On August 7, 1904, he became very constipated, not having had a bowel movement for fourteen days; at the same time he had considerable abdominal pain. After evacuation of the bowels by means of purgatives, the pain subsided but still lingered. About one month later his right leg suddenly gave way while walking, associated with cramp-like pain. The pain persisted two days, and then the right leg became totally paralyzed. One week later the left leg was similarly affected but without pain. Again he became very constipated and had some difficulty in urinating. Since that time the patient has been confined to bed, and he says that he has not been able to feel anything in either lower extremity. Occasionally he had girdle sensation.

The following notes were made on the day of admission: The patient is fairly well developed. He can wrinkle his forehead evenly on both sides. The nasolabial folds are of equal prominence, he can show teeth, whistle, and draw mouth back on either side. The masseter and temporal muscles contract promptly. There seems to be some wasting of the face but it is symmetrical. Both pupils are round and equal and react promptly to light and accommodation. Sensation for touch and pain is normal over the face and neck. The extra-ocular muscles are normal. Motion

and resistance to passive movements and grasp of hands is good on both sides. There is very slight ataxia of both upper limbs as shown by the finger to nose test. Sense of position is normal on both sides and sensation for touch, pain, heat, and cold is normal in the upper limbs. The lungs are hyper-resonant anteriorly and harsh breath sounds are heard over the upper portions. No rales can be elicited. The heart is normal. The abdomen is somewhat distended but not tympanitic. Palpation elicits no pain or tenderness. The abdominal organs seem normal. Sensation for touch and pain is normal over chest and abdomen; sensation for heat and cold is normal down to a point two inches below the umbilicus but below this level thermal sense is lost. There is marked atrophy of both lower limbs. Motion and resistance to passive movements is nil in both limbs. Patient is unable to move even toes. There is double foot drop. Impossible to test for ataxia on account of paralysis. Both limbs are slightly spastic, the left more so. At intervals there are involuntary contractions of the flexor and adductor muscles of each thigh. The right knee jerk is exaggerated, the left seems normal or slightly decreased. Ankle clonus is present on both sides, but it is much more persistent on the right. Babinski reflex is distinct on both sides. Sensation to touch is normal, on the left limb except for space extending downward six inches from the middle of the leg from that point downward it seems to be diminished, on the right side it is present, but the man is unable to locate touch on leg. Sensation to pain is present on the right limb but is diminished and he is unable to locate pin pricks. Sensation to pain on the left side is about the same as on the right. Sensation to heat and cold is absolutely lost over the whole of both lower extremities. Achilles jerk is absent on the right, but present on the left.

Two days later a slight angular deformity was discovered corresponding to the ninth thoracic vertebra. On November 22, all forms of sensation including touch, pain, and temperature were lost over both lower extremities and extended upward as far as the level of the umbilicus. A large bed sore had developed over the sacral region. The patient died November 30. The autopsy was performed the next morning.

Anatomical Diagnosis. Bilateral pleural adhesions, obliterative pericarditis, chronic fibrous tuberculosis of the lungs, malposition of the left kidney, gastrectasis, and enteroptosis, miliary tuberculosis of liver, dilatation and ulceration of œsophagus, subphrenic abscess, caries of lower thoracic vertebræ, tuberculous external pachymeningitis, internal hydrocephalus.

Microscopic examination of the lower thoracic segments where the pressure was greatest showed that the outline of the cord was not altered. The pia was slightly thickened on the anterior aspect, the adventitia of the pial vessels was less compact than normal

and was infiltrated with small round cells. Here and there the pia was separated from the cord, the spaces between containing a few round cells and red blood corpuscles. In the white matter the neuroglia cells were swollen and increased in number; and the glia septa were thickened, standing out prominently. Many granular cells and a few round cells were seen diffusely scattered. The white matter presented the characteristic vesicular appearance. The medullary sheaths were distended, many axis cylinders had entirely disappeared and others were swollen or atrophied. The bloodvessels were thickened and there was moderate perivascular round-cell infiltration. Although the white substance was severely diseased the area of the lateral pyramidal tracts was perhaps more affected than the other parts. The central portions of the gray matter were entirely destroyed, including all of the gray commissures and part of the anterior horns, leaving a large irregular cavity with ragged edges containing debris, few small round cells, red blood corpuscles and compound granular cells. In the remaining portions of the gray matter there were scattered round cells and an occasional granular cell. Here the bloodvessels were also thickened, and there was moderate perivascular infiltration. The necrotic cavity did not extend beyond the limits of the eighth dorsal segment but the central canal in the adjoining sections above and below was distended and the ependyma cells were partially destroyed.

In the upper dorsal, cervical, and lower lumbar segments there was some thickening of the bloodvessels within the gray matter and slight perivascular infiltration. This was more marked in the branches of the anterior spinal artery near the base of the anterior horns. With the Weigert method there was degeneration of Goll's column extending upward into the cervical region. In the lower lumbar segments no distinct degenerations were found. At the level of compression many ganglion cells within the gray matter had been destroyed but a few remained which appear swollen, and with the Weigert stain the nuclei were indistinct. The Nissl stain could not be used. The bloodvessels of the pia about the pons and medulla seemed somewhat thicker than normal and some showed slight perivascular infiltration. The cells of the choroid plexus about the fourth ventricle were very much swollen and the bloodvessels were thickened. Sections of the cerebral cortex presented some rather doubtful round cell infiltration of the pia.

Case II.—J. D., was admitted July 16, 1904, to the service of Dr. Spiller, complaining of paralysis of both lower extremities. Three years previously his left leg had been amputated six inches below the knee as a result of injury. He denied syphilis. His family history was negative. July 2, 1904, he was compelled to go to bed on account of severe dull aching pain just below the

angle of the scapula. Two days later there was much numbness and tingling just below the painful areas and on that day he suddenly lost power in both lower extremities. During this time he had had retention of urine and was constipated.

The following notes were dictated two days after his admission: The patient is fairly well nourished. Pupils are round and equal and react promptly to light and accommodation. The extra-ocular muscles are normal. Facial muscles contract equally and promptly; movements of upper extremities are equal and normal. The epigastric and abdominal reflexes are absent on both sides. Cremasteric reflex is absent on the left and diminished on the right. The knee jerks and Achilles jerks are absent on both sides. There is no ankle clonus on either side. Sensation for pain and touch is lost over both legs and abdomen up to a point two and one-half inches below the right nipple, and about one inch lower down on the left side. Adjoining this line above is a zone of hyperesthesia about two inches wide, which narrows to about one inch in width near the axilla of either side. Testicular pain is absent.

The following additional notes were dictated by Dr. Spiller some days later: Sensation for touch, pain, and temperature is similar to the above. Cremasteric reflex is present on both sides but diminished. Passive movement of the stump of left leg on thigh causes involuntary jerking movement of this limb of which the patient is not conscious without seeing it, but he is conscious of a jarring sensation in his back. These involuntary movements are not distinct in the right lower limb. He has no knowledge of the sense of position of his legs. The knee jerks are both absent, the plantar reflex is present on the left side, but sluggish on the right. There is an area of tenderness of the spinous processes about the level of the spines of the scapula, but no deformity.

The patient died July 28, 1904.

Macroscopic examination of the spinal cord and its membranes showed an external pachymeningitis extending from the lower cervical region to the upper lumbar. There was a considerable amount of necrotic cheesy material which by microscopic examination revealed the characteristic picture of tuberculous disease. Microscopic examination of sections taken from the upper thoracic portion of the spinal cord showed no diminution in its volume. When stained by the hemalum and fuchsin method there was slight cellular infiltration of the pia, and the pial vessels presented slight infiltration of the adventitia. In the white substance there were numerous vacuoles, mononuclear cellular infiltration, thickening of the bloodvessels and slight perivascular infiltration. The neuroglia cells were increased and here and there were a few granular cells. The anterior portions of the posterior columns were partially destroyed. The anterior longitudinal septum was infiltrated

with round cells and appeared more prominent than normal. In the gray substance there was moderate diffuse cellular infiltration of the mononuclear type and red blood cells as well as compound granular cells were found. The blood vessels which were cut in cross section appeared thickened, and the perivascular and perigangliar spaces were enlarged. The most marked inflammatory changes were found about the gray commissures and central portions of the anterior horns. In some sections necrosis has taken place in the area supplied by the commissural branch of the anterior spinal artery. With the Weigert method the posterior and lateral columns suffered most, and the anterior columns least. Axis cylinders had disappeared and many remaining were swollen, while here and there a few normal fibers were seen. Many of the ganglion cells of the anterior horns had disappeared, others stained poorly, and their nuclei were indistinct. In the lower thoracic lumbar and cervical segments the process was similar in the gray matter, but much less marked, while the white substance was little affected. Distinct tract degeneration was absent except for a few degenerated fibers of Goll's column. Sections of the medulla in its lower part showed very minute capillary hemorrhages chiefly in the gray matter. The brain was not examined.

Case III.—C. M., a white female, aged fifty years, was admitted to the Philadelphia Hospital in the service of Dr. Spiller complaining of weakness of the lower limbs. Syphilis was denied. Three months previous to admission patient first developed some pain about the left shoulder which resisted all treatment. About two months later both legs began to grow weak, this gradually progressed until one week before admission when she was unable to walk or stand without assistance.

Physical Examination: The patient is much emaciated. The pupils are equal and react normally to light and accommodation. Movements of muscles of the face, tongue, larynx, and pharynx are normal. The power of the upper extremities is equal and normal. Triceps and biceps jerks are equal and normal. Both lower extremities are completely paralyzed and there is extreme contracture at the knees and hips. From time to time there are violent jerking movements at the knees. Patellar tendon reflex is normal on the left, but slightly decreased on the right. Achilles reflexes are equal and normal. Clonus is absent. There is distinct Babinski signs on both sides. Sensation for pin prick and for touch is lost over both lower extremities and abdomen as far as the fifth interspace, at this point pain and tactile sensations are impaired but not lost. Sensation for heat and cold was not tested. The vertebral column although prominent on account of emaciation showed no deformity.

Macroscopic examination showed tuberculous caries of the second thoracic vertebra and an external tuberculous pachymenin-

gitis beginning one quarter of an inch above the exit of the second thoracic root and extending one quarter of an inch below the exit of the third thoracic root, therefore involving the whole of the intradural portion of the third thoracic root from its exit from the cord to its exit through the dura. Microscopic examination of section taken from the third thoracic segment showed no change in contour. When stained by the hemalum and fuchsin method the pia seemed normal, but there was a slight mononuclear cellular infiltration of the adventitia of some of the pial vessels. In the white matter the walls of the bloodvessels were thickened and there was a very slight perivascular infiltration of mononuclear cells and an increase of the glia cells. There were no distinct areas of softening.

In the gray matter there were many mononuclear cells diffusely scattered. By the Nissl stain the ganglion cells were few in number and those remaining were much degenerated. With the Weigert method the medullary sheaths were swollen and many axis cylinders had disappeared. By the Marchi method nearly all the fibers of the white matter were degenerated, but a few scattered normal fibers still remained on the lateral columns near the periphery. Above and below the site of compression distinct tract degeneration was absent, though a few fibers were found staining very darkly in the pyramidal tracts and in the posterior columns by the Marchi stain.

In cases of tuberculous caries infection is generally carried to one of the vertebræ from some other focus within the body such as the lung, and a chronic osteomyelitis or periostitis ensues. This may go on to necrotic softening, and then by purely mechanical means the adjacent vertebræ above and below become approximated producing the well-known deformity of Pott's disease. In some instances this deformity may be sufficient to cause direct pressure upon the cord, but as Kraske has shown, it is uncommon; he having found it in only 6 of his 58 cases. Occasionally a subperiosteal abscess may exert pressure; Oppenheim and others have even seen cases in which spicules of necrotic bone encroached upon the cord. In the great majority of cases however, infection extends to the external lateral and posterior surface of the dura setting up a chronic inflammation which produces great thickening with epidural exudates and fungoid proliferations. Fickler in 20 cases found compression caused by dislocation of a vertebra in 9 per cent.; by abscess formation, in 17 per cent.; while pachymeningitis externa was responsible for 73 per cent. Infection of the dura nearly always arises by direct extension from a focus in one of the vertebræ, yet Schlesinger, Henneberg, and Rossi, have each reported a very uncommon condition in which there was tuberculous pachymeningitis without caries of the vertebræ.

A similar case has recently been under the care of Dr. Spiller, and Dr. Frazier, the notes of which are as follows:

CASE IV.—H. B., a male, white, was admitted to the University Hospital, April 10, 1909, in the service of Dr. Spiller.

The patient's father, grandfather, one aunt, and one sister died of tuberculosis. Six years ago the patient had scarlet fever which was followed by paralysis of all four extremities lasting two months and then he entirely recovered. Seven months previous to admission he first developed pain in the region of the sixth dorsal vertebra. Pain was present on movement and on jarring of the spinal column, and continued in spite of treatment. About five weeks ago he noticed his legs were growing weak and that he staggered when walking. Occasionally he had cramp-like pains in the calf muscles of both legs. This condition increased gradually until two weeks ago when he was not able to walk at all. Pain still continued in the lower legs. Patient cannot control bowels and can retain urine only a short time, and is troubled with distention of the abdomen. He states that for the last four weeks he could not feel distinctly below the hips.

The following notes were dictated by Dr. Spiller: Patient is completely paralyzed in both extremities, slight movement of drawing upward of the left lower leg seems to be from muscles of the trunk. Limbs are not wasted. Patella and Achilles reflexes are about normal on each side. No ankle clonus on either side. Dr. Willard, Jr., noticed bilateral ankle clonus three days ago, before patient entered hospital. Tactile sensation seems to be preserved in all parts of the body except possibly over the front and outer side of the thighs. Here he sometimes answers incorrectly. Pain, heat, and cold sensations are lost or greatly impaired over both lower limbs and trunk anteriorly and posteriorly to a line three inches below the nipple. Area of disturbed sensation shades off gradually into an area of normal sensation. Babinski sign is typical on each side. Testing him with pin prick, or heat, and cold, causes at times either lower limb to be forcibly drawn upward. The upper thoracic vertebræ are distinctly arched, but there is no sharp kyphosis, only gradual arching. Von Pirquet tuberculin test was positive, twenty-four hours. Urine was negative. Blood count was: hemoglobin, 48 per cent.; red blood corpuscles, 4,880,000; leukocytes, 11,900.

Additional notes dictated by Dr. Spiller, May 19, 1909: Both legs are completely paralyzed. There is considerable desquamation of the skin of the feet and legs below the knee. There is involuntary drawing upward of lower limbs at hips and knees. Has imperfect control over bladder, cannot hold urine; no control over rectum. Only pain he has now is at lower costal margin, and there is no atrophy of any part of the body or even of the lower limbs. Lower limbs are very spastic. Knee jerks are

exaggerated on both sides. Patellar clonus present on both sides. Achilles jerks are exaggerated on both sides but clonus is not obtained on either side on account of spasticity. Any irritation of the limbs or trunk causes limbs to be drawn forcibly upward. Touch, pain, heat, and cold sensations are lost in the lower limbs and trunk anteriorly and posteriorly to a line drawn around the body from the eleventh and twelfth thoracic vertebræ to the sixth interspace on the left side in the nipple line, and seventh interspace on the right side in the nipple line. This line is very sharp for touch but not so sharp for pain and temperature sensations. There is no involvement of the upper limbs. Prominence of vertebræ is in the midthoracic region but no actual displacement.

On June 24, Dr. Frazier removed the fourth, fifth, and sixth dorsal spinous processes. During the operation the following notes were dictated. Coming out between the transverse processes of the fifth and sixth dorsal vertebræ was found a mass of tissue about the size of a marble presenting the appearance of granulation tissue. Upon exposure of the cord it was found free from involvement, the tumor tissue seemed to come out from either right side of the body of the vertebra or from the transverse process of the fifth dorsal. All tumor tissue that could be was removed with scissors and curette. There was evidently compression of the cord at the site of injury which was relieved by removal of the laminæ. Tumor did not make pressure over the dorsal but over the lateral aspect of the cord. Recovery after operation was good.

The pathological report was as follows: The specimen consists of laminæ and small portion of spinal meninges with nerve cord about three inches long. Microscopically, soft tissue removed from laminæ shows simple areolar tissue, the fibrous elements of which are somewhat thickened and in places infiltrated with small round cells, also a few degenerated muscle fibers are seen and many typical tubercles were found with epithelioid cells and giant cells.

On October 11 examination of the patient showed there was no return of power in the lower extremities. Sensation to pain and touch is lost below the fifth interspace on the right side anteriorly and the sixth space anteriorly on the left side. Patient complains of sharp pain in the region of the right nipple on attempting to raise head from bed.

In attempting to explain the intraspinal lesions of Pott's disease it must be borne in mind that there are two cardinal factors each of which originate outside the dura, namely, pure mechanical compression and infection. Charcot and Michaud believed that degeneration of the spinal cord was caused by infection extending into the substance of the cord setting up a secondary myelitis;

on the other hand, Kahler was able to show by compressing the spinal cords of animals with non-toxic substances that lesions similar to those following caries of the vertebræ resulted. Later Leyden, recognizing the possibilities of infection, declared that compression in itself was an important factor. Strümpell strongly opposed the myelitic theory explaining the alterations in the cord as the result of œdema stoppage of the lymph stream, and anemia, secondary to pure compression; Schmaus was inclined to accept Strümpell's view but modified it somewhat by adding that there was a collateral inflammatory œdema which could be attributed to toxic influences; more recently, however, in an article upon myelitis the same author has expressed the opinion that constant prolonged pressure upon the cord may lead not to stasis œdema but to true secondary inflammation, that is, myelitis.

The first three cases which I have described presented swelling and destruction of axis cylinders, proliferation of the glia, round-cell infiltration, sclerosis of the bloodvessels, perivascular infiltration, necrotic softening of the central gray matter, and compound granular cells at the level of greatest compression of the spinal cord. In Case I there was an internal hydrocephalus affecting only the lateral ventricles; the formina, however, were not occluded, but the cells of the choroid plexus were decidedly diseased; it is conceivable, therefore, that as a result of perverted function of diseased cells there may have been an increase of secretion sufficient to cause this distention. But it is also possible that hydrocephalus may have been the result of compression of the cord, and that if an ophthalmological examination had been made choked disk would have been found. Choked disk has not been seen frequently in Pott's disease, yet it has been observed in spinal tumor by Bailey. At other levels of the spinal cord where compression seemed to play no part there were definite though very moderate signs of vascular disease, consequently it might seem as if there was some other element responsible as well as compression.

Spiller in an article on Pott's disease refers to a form of simple meningomyelitis without giant cells or miliary tubercles, occurring particularly when Muller's fluid had been used for preservation, he also quotes Oppenheim who had called attention to a similar type of myelitis in persons dying of generalized tuberculosis. In my cases there were no specific signs of tuberculosis found within the dura, yet the diagnosis of Pott's disease is evident, and it does not seem probable that the existence of myelitis would be disputed.

The symptoms of cord involvement in Pott's disease vary considerably in their mode of onset, but after having once begun they frequently progress rapidly. Usually the onset is chronic, the signs of paralysis requiring some months to reach their height. Occasionally paraplegia develops in the course of two or three weeks. Very rarely, however, there is an instantaneous onset,

and, moreover, in such cases there is usually a history of trauma, or some undue strain upon the diseased vertebral column immediately preceding the initial paresis or paralysis, which causes sudden displacement of one of the vertebræ and thus brings about rapid compression of the spinal cord. Gowers describes a child with angular deformity of the spine, who, while walking across the room, suddenly fell to the floor and after being lifted up was paralyzed in both legs. In Case IV not only was deformity absent, but, as far as could be determined at operation, the vertebræ were entirely normal. Deformity was entirely lacking in the other three cases at the time of the onset of paraplegia, yet in Case I and Case II the development of paralysis could not have been more rapid. In the first case, motor and sensory paralysis of one lower extremity was said to have begun instantaneously, the patient's right leg suddenly giving way under him while walking, and one week later the left leg was similarly affected. The second patient developed paralysis of both lower extremities in an equally rapid manner. Truly an apoplectiform onset in the strictest sense of the term.

After searching the literature upon this subject I have been able to find only two cases described in which paralysis developed instantaneously without deformity of the vertebræ. One case with necropsy reported by Raymond seventeen years ago seems to have been entirely overlooked, another without necropsy was described by Martineck during the past year. Raymond's case is as follows: A young girl developed complete motor paralysis of both upper extremities and incomplete motor paralysis of the lower limbs within a few hours. Laminectomy was performed and the pia was found to be thickened and the cord much congested, but without evidence of compression. The patient died on the same day and at the autopsy tuberculous caries of the third cervical vertebra and abscess formation was found. Microscopic examination showed inflammation and hemorrhage in the gray matter, sclerosis of the bloodvessels and cellular infiltration of the pia, while the white matter was much less involved, yet there were no specific lesions of tuberculosis within the dura.

Martineck's case was that of an adult male, who had been complaining for some months of severe pain. The patient went to bed feeling generally weak, the next morning there was paresis of both legs, by the afternoon there was paralysis of both lower extremities. When the patient was seen at the hospital the following day there was almost complete motor paralysis and involvement of the bladder, still the vertebral column showed no abnormality. There was neither tenderness nor pain on movement. It was not until eight days after paralysis had developed that an angular deformity was discovered extending from the eighth to the eleventh dorsal vertebræ. *X*-ray examination showed abnormality in the position of the ninth dorsal vertebra.

When the term myelitis is used in its strictest sense to mean inflammation of the spinal cord, Russel believes that it is a rare disease, and attributes much of which we speak of as myelitis to softening consequent upon vascular occlusion, in which inflammation plays no part, unless it is some inflammatory process in connection with the walls of the bloodvessels which tends to thrombosis and later softening. Douglas Singer also refers the majority of cases of myelitis to primary thrombosis.

It is well known but perhaps not thoroughly appreciated, that in cases of syphilis occlusion of some of the smaller spinal vessels produce sudden weakness and paralysis; in fact, sudden onset of paralysis is common in syphilitics. Spiller, in an article upon syphilitic acute anterior poliomyelitis due to thrombosis, emphasizes the importance of considering the rapid development of paralysis and says "spinal thrombosis is not a rare condition and is probably the cause of most of the apoplectiform palsies that occur in myelitis." In my case, syphilis, dislocation of vertebræ and trauma can all be excluded with certainty, yet a traumatic cause, if this expression is permissible, was present, that is to say compression. As has been already pointed out, compression of the spinal cord even when slight, can in itself cause œdema and inflammation with thickening of the bloodvessels within the cord, in other words, a fertile soil for thrombosis. Epidural inflammation and fungoid proliferations increase very gradually up to a certain point without evident disturbance in the functions of the cord unless it be pain; but when this point has been reached a very minute sudden increase may be sufficient to give signs of rapidly developing weakness or palsies, on the other hand, it is possible that it is just at this stage of the disease that thrombosis develops. Whether or not in my cases the initial palsies were caused by sudden increase of pressure with thrombosis, or to increased pressure without thrombosis, or to the changes which were found within the cord, is of course, problematical.

Raymond was inclined to look upon his case as one of hematomyelia, also Huber and Vorkarstner in discussing Martineck's case suggested the possibility of there having been a hemorrhage within the gray matter of the cord in addition to compression. Spontaneous hemorrhage in the spinal cord is exceedingly rare. Minor who has studied this question minutely, says that among all the cases which he has observed (other than Pott's disease) hemorrhage occurred only twice without preceding trauma. In an anatomical sense it is always difficult to make a sharp distinction between primary hemorrhage with subsequent myelitis from primary hemorrhagic myelitis and in many instances absolutely impossible.

In Cases I and II it was impossible to prove conclusively that thrombosis had taken place, nevertheless on account of marked thickening of the bloodvessels throughout the cross section of the

cord, together with extensive central softening and similarity of the onset of paralysis to cases of primary myelitis in which thrombosis has been proved, it seems more than probable that thrombosis may have occurred. At all events, instantaneous paralysis in Cases I and II and the more slowly developing paraplegia in Cases III and IV was the clinical expression of an intense myelitis and was beyond all doubt the direct result of compression of the spinal cord by means of tuberculous external pachymeningitis.

In determining the upper limits of a focal lesion causing compression of the cord, particularly when situated in the dorsal region, there is always more or less uncertainty. The most important single sign is the character and extent of sensory loss of function. Certain authors rely upon the level of hyperesthesia so frequently found just above the level of the total loss of sensation. In an article on spinal tumors Bailey maintains that the upper limits of incomplete loss of sensation is probably the most accurate guide in determining the exact level of the lesion. In two of my cases the lesions were too diffuse to draw accurate conclusions, but in Cases III and IV the limits of hypesthesia of the skin indicated quite accurately the segment of the cord which was involved.

The diagnosis of Pott's disease when deformity of the spine is present is generally easy, but, as Moussaud has pointed out, without this characteristic sign an accurate diagnosis may be exceedingly difficult or impossible. Fortunately, cases of this kind are uncommon, yet unmistakable evidence of caries is by no means always present. Nevertheless by a careful consideration of the clinical history, bearing in mind the similarity of the onset of paralysis in certain cases of Pott's disease with that of other form of myelitis particularly in syphilitics, and by use of *x*-ray examinations, tuberculin test, the Wassermann and Noguchi reactions, and lumbar puncture, in a certain number of cases at least, an accurate conclusion can be reached. If in a given case it can be proven that the bones of the vertebral column are not involved and the initial paralysis did not begin suddenly operation should be seriously considered. In such cases it is probable that the symptoms are caused by slowly increasing pressure upon the cord by a dry inflammatory exudate with a minimum amount of pus, or pus may be entirely absent as in Case III; therefore, if operation is done early and pressure removed recovery might be possible. Recovery does not seem to occur without operation. On the other hand, an apoplectiform onset of paralysis would indicate serious intraspinal lesions and operative interference might be of no advantage, and yet it is probable that in these cases also, compression is the primary etiological factor; if, therefore, it can be removed by operation, the injured cord will have better opportunity to recover its normal function, although in Case IV operation was of little benefit.

BIBLIOGRAPHY

Bailey. Jour. of Nerv. and Men. Dis., May, 1910.
Charcot. Leçons sur les Maladies des Système Nerveux, Paris, 1885.
Fickler. Deutsch Zeitschrift für Nervenheilkunde, 1900, vol. xvi.
Gowers. Diseases of the Nervous System, 1907, i, 291.
Henneberg. Centrl. für Nerven. und Psych., 1903, vol. xiv.
Kahler. Prager Zeitschrift für Heilkunde, 1882.
Kraske. Archiv für klin. Chirurgie, vol. xli.
Leyden, Goldscheider. Die Erkrankungen d. Rückenmarks und d. Medulla Oblongata, Wien, 1907.
Michaud. Sur la Myélite et la Méningite dans le Mal Vertebral, Paris, 1871.
Moussaud. Thesis, Paris, 1906.
Martineck. Berlin klin. Wochenschrift, 1909, vol. xli.
Minor. Handbuch der pathologischen Anatomie des Nervensystems, ii, 1031.
Oppenheim. Lehrbuch der Nervenkrankheiten, 1908, vol. i.
Raymond. Revue Neurologique, 1893, p. 98.
Rossi. Archiv d. Neurol., 1906.
Russell. Lancet, 1906, vol. ii, 1.
Schlesinger. Beitr. zur. Klinik. d. Rückenmarks und Wirbeltumoren, Jena, 1898.
Schmaus. Die Compressionsmyelitis bei Caries d. Wirbelsäule, Wiesbaden, 1889.
Schmaus. Deutsche Zeitschrift für Nervenheilkunde, 1904, vol. xxvi.
Singer. Quoted by Leyden and Lazarus. Diseases of the Nervous System, edited by Church, 1908.
Spiller. Bulletin of the Johns Hopkins Hospital, June, 1898.
Spiller. Journal of Nervous and Mental Diseases, 1909, vol. xxxvi.
Strümpell. Lehrbuch d. spec. Pathologie und Therapie, 1892.

THE PATHOLOGICAL FINDINGS IN THE PARATHYROIDS IN A CASE OF INFANTILE TETANY.

By B. S. Oppenheimer, M.D.,
ASSISTANT PHYSICIAN TO THE DISPENSARY OF MT. SINAI HOSPITAL, NEW YORK.

(From the Children's Service of Dr. Koplik, Mount Sinai Hospital, New York.)

In the year 1880, the Swedish anatomist, Sandström, first described the parathyroids in man and also in the horse, cattle, cat, dog, and rabbit. In the same year, Nathan Weiss gave the first description of three cases of tetany after thyroidectomy; the condition was at that time called tetania strumipriva. Today, after thirty years, it is generally considered that such tetany, whether operative or experimental, is due not to the loss of the thyroid, but to the removal of the parathyroids (Vassale and Generali, Biedl, Pineles, Erdheim). In other words, the condition is not a tetania strumipriva, of the same origin as myxœdema and cachexia strumipriva, but a tetania *parathyreopriva*.

In regard to the so-called medical or spontaneous tetanies, however, it is at present still merely an hypothesis[1] that they are due to insufficiency of the parathyroid. Among such spontaneous tetanies

[1] For opposition to this theory see Berkeley, Forsyth, Kassowitz, and Thompson.

are included: The idiopathic workman's tetany, gastric tetany, tetany of pregnancy and lactation, of acute infectious diseases, and finally, children's tetany. The identity of all these clinical forms has not been established, but there are several symptoms common to them all, especially the electrical and mechanical irritability of the peripheral nerves. As regards their pathogenesis, there are some observations to indicate that the tetany of pregnancy and lactation may be due to parathyroid insufficiency (Vassale, Pineles, Erdheim, Adler and Thaler). For children's tetany, it has been the Viennese school (Escherich, Erdheim, and their pupil, Yanase) which has been most active in investigating the parathyroid in its relation to tetany and tetanoid conditions (spasmophilia). The recent view may be summarized about as follows: For all tetanies, operative, experimental, or spontaneous, a tetany toxin due to some disturbance in metabolism (possibly in calcium metabolism[2]) is presupposed. It is assumed to be a function of the parathyroid to neutralize such a tetany poison. If these glands through some functional or organic change are unable to neutralize this toxin, then the latter can act on the nervous system and produce the group of symptoms called tetany.

On looking for an anatomical basis for children's tetany, Escherich and his followers found hemorrhages or residua of hemorrhages in the parathyroid of children not uncommon, indeed in 33 out of 89 autopsies made by Yanase. These hemorrhages are thought to originate from intrauterine asphyxia, or some intrapartum injury.

Fifty of Yanase's 89 cases were tested as to their electrical irritability; none of the cases showing normal electrical reaction had hemorrhages in the parathyroid; all under one year showing electrical hyperexcitability presented evidences of hemorrhage. (After the lapse of one year all evidence of a prenatal hemorrhage of the parathyroids may be lost.) Among all Yanase's cases only 1 was a manifest tetany, 1 was merely tetanoid, 9 more were cases with convulsions. Below will be found a table of all the published cases of manifest tetany in children in which the parathyroids were examined; and in addition, a few important cases of allied conditions.

In America tetany in children is either less common than in certain parts of Europe or has escaped recognition. Perhaps with the more extended use of that essential guide to the diagnosis of infantile tetany and spasmophilia, the electrical examination, more cases will be discovered in the future. At any rate, up to the present, no pathological examination of the parathyroids of a fatal case of children's tetany has been published in this country.

[2] See for disturbances of calcium metabolism Erdheim, Hecker, Kassowitz, Leopold and Reuss, MacCallum and Voegtlin, Musser and Goodman, Parhon and Urechie, Parhon, Dumitresco, and Nissipesco; also the views of Berkeley and Beebe, and Pexa.

TABLE OF PUBLISHED CASES OF MANIFEST TETANY IN CHILDREN IN WHICH THE PARATHYROIDS WERE EXAMINED.

Investigator.	Clinical diagnosis.	No. of cases.	Age.	Pathological condition of the parathyroid.
Erdheim	Tetany	3	3½, 5, 8 months, respectively	Hemorrhage
Escherich	Tetany in the course of tuberculous meningitis	1	7 years	Degeneration
Yanase	Tetany and meningitis	1	2½ years	Hemorrhage
	Tetanoid	1	3½ months	Hemorrhage
	"Krampfe"	9	1 day to 5 months	8 cases hemorrhage
Königstein	Tetany	1	9 months	(1) Marked reaction with iodine and Best's glycogen method. (2) Increase in size
Harnett	Death with convulsions 12 hours after food-poisoning with diarrhœa, etc.	1	3 years	Congestion and minute traces of fat
Thiemich[3]	Spasmophilia (not manifest tetany)	3	4, 11, 12 months, respectively	Negative
Forsyth	Tetany	1	Infant	Negative. Found only three parathyroids

The following is a report of such a case of manifest infantile tetany with the electrical examination and a description of the pathological findings of the four parathyroids:

Clinical History. B. J., aged eight months, was seen by Dr. Koplik February 23, 1909, in consultation with Dr. S. There were three other children in the family, all healthy and well. The patient was a well-nourished, bottle-fed infant. She had been well up to five days before the consultation, when without any known cause the child was taken with convulsions, which were repeated at short intervals. On the day of the consultation there had been one convulsion which had been controlled.

On examination, the child was easily startled in its crib, looked pale though well nourished, had very slight signs of a rachitic rosary, especially about the costochondral junction, no craniotabes, no marked enlargement of ends of the radii; there was no fever; fingers and hands were held in the typical accoucheur position, the forearm slightly flexed on the arm, the toes were strongly flexed, and any attempt to extend them painful. Examination otherwise was negative.

The diagnosis of tetany was made and the patient put under appropriate treatment.

The child was lost sight of until March 29, 1909, when it was admitted to the hospital with the following history:

The patient was born after an instrumental delivery; there were no paralyses, no convulsions. Infant was bottle fed from birth; its bowels at first were constipated, but now moved freely and were soft in consistency. No vomiting. No infectious diseases. About ten weeks ago patient was taken with fever and cough,

[3] The cases of Thiemich have been criticised as not conclusive in several respects, apparently with justice; for example, in none of his cases did he find more than three glands.

which lasted for two weeks. Then it improved and was apparently well until six weeks ago.

The present illness began six weeks before admission to the hospital, when the child had convulsive attacks, which continued up to the time of admission. In these attacks the child at first seemed unable to get its breath; then had rigidity of the thumbs, which were flexed; the forearms were flexed; child became blue. These attacks lasted from two to five minutes; no cough. Between the attacks at times there were crowing sounds at the beginning of crying. Bowels continued normal.

The general condition on admission was excellent; the child's color was good; the head was well formed, the fontanelle open about one-half inch; no cranio-tabes; no rigidity of the neck; no MacEwen sign; the ears were negative; the pupils of the eyes were round and equal, reacted normally to light; there were no teeth; gums in excellent condition, tongue was clean; there was slight hypertrophy of the tonsils, thymus could not be percussed; there were no enlarged glands; the chest was well formed and symmetrical; there was a slight rachitic rosary as noted above; the heart presented nothing abnormal; the abdomen was normal, slightly tympanitic; the liver did not extend below the free border of the ribs; the spleen was not palpable.

March 30, 1909. When the child was seen by Dr. Koplik, the fingers and the arms were held in a typical tetany position, and the toes were held stiffly and were strongly flexed. The child cried just as on the first consultation, when attempts were made to straighten the toes. There was a Chvostek phenomenon, but the Trousseau phenomenon could not be elicited. The child had an anxious expression. It had had no convulsions since admission. On the same day the ulnar nerve was tested with the galvanic current to determine its electrical reactions. It was found that there were cathodal opening and closure contractions, and anodal opening and closure contractions to a current of less than three milliampères. The anodal opening contraction was greater than the anodal closure contraction. (In other words, Erb's phenomenon of electrical irritability was established by the method of von Pirquet.)

April 1. The child showed contractures of the fingers and marked flexion of the toes; had had distinct attacks of laryngismus stridulus since it had been in the hospital, but no convulsions.

April 3. There had been frequent attacks of laryngismus stridulus, the infant was restless and had an anxious expression. The forearms were slightly flexed on the arms, fingers held in the tetany position and legs slightly flexed on the thighs. At 10.30 A.M. the nurse noticed that while crying the child suddenly became cyanosed and rigid. This lasted about two minutes, after which the baby appeared to be exhausted (tetany convulsion).

April 4. Child continued in very good general condition. In the previous twenty-four hours the typical tetany position had become very marked and then the fingers and toes had relaxed partly. A number of attacks of laryngismus stridulus had occurred with crying. About 4 P.M. the child suddenly became very pale, somewhat cyanotic, restless, apparently had a convulsion, and died in less than half a minute. Unfortunately the nurse gave no history as to whether the child had an attack of laryngismus just preceding this fatal seizure.

The patient was in the hospital seven days, and in that time the temperature ranged from 98.5° to 99.8°; the pulse was regular, 128 to 140 on admission, to 126 and 128 after admission. The child took its nourishment, from 33 ounces to 48 ounces daily, had one to three bowel movements of good color and consistency, and had a weight of 16 pounds 10 ounces.

On the first day of admission there were no attacks of laryngismus, but every subsequent day there were laryngismus attacks that were not alarming.

Pathological Findings. Autopsy 1774. B. J., aged eight and one-half months; died April 4, 1909, at 5.30 P.M.

Wound examination April 5, 1909, at 1 P.M.

As no autopsy was permitted, only a small incision in the neck was made. Through this, the larynx, trachea, thyroid, œsophagus, heart, and lungs were removed.

The larynx, œsophagus, and thyroid were negative. The thymus weighed 22 grams. Its length, after removal, was 7 cm. The ductus arteriosus permitted the passage of the finest probe. The foramen ovale was closed. The heart was negative. The aorta was normal in width. The left lower lobe of the lung was adherent; otherwise negative.

Microscopic Examination. Thyroid: The interstitial connective tissue was very prominent. Thymus: Negative.

Parathyroid Glands. Macroscopic features: Four parathyroids (the normal number) were found; two of these were recognized on gross examination, the other two were discovered by dissection and microscopic examination of all the tissue in the neck which in any way resembled the parathyroid gland. Macroscopically the two glandules discovered with the naked eye were pale pinkish brown in color and nowhere showed any punctate elevations or irregularities of the surface which might have indicated hemorrhages.

Histological Features. The material was fixed in alcohol, embedded in paraffin, and serial sections 5 microns thick were cut and stained, most of them with hematoxylin; some with eosin-hematoxylin for colloid and oxyphil cells; some with ferrocyanide of potassium and hydrochloric acid for hemosiderin; and some with Gram-Weigert's stain for bacteria.

The histological features may be divided into: (1) Such as are normally found in infantile parathyroids; and (2) such as are unusual or pathological and might in some way account for or be associated with the tetany.

The parenchyma of each of the four parathyroids as may be seen in the plates, consisted entirely of the so-called principal cells, that is, of polyhedral, epithelial cells with clear or very faintly stained cytoplasm, and with a round or oval, sharply-defined, deeply-stained nucleus. In many parts of the glandules these cells were grouped in a compact mass as is usual in an infant parathyroid, and in many other parts the cells were arranged in strands or columns. The columns, one to eight cells deep, were separated from one another by vascularized connective tissue. The cytoplasm of most of the epithelial cells was either not stained at all or very faintly stained by means of eosin and hematoxylin. In some other of the principal cells the cytoplasm had a pink non-homogeneous appearance when stained with eosin. The cell membrane of the principal cells was sharp and well defined. The nuclei were comparatively large, deeply stained, and stood out prominently with sharp, round or oval outlines. The nucleoli and chromatin were well stained. The chromatin was granular and in the form of a network. In only one instance were the epithelial cells arranged in the shape of an acinus, with a central clear "vesicle." In several places the valves, first described by Yanase for the parathyroid glands, were found in the larger veins (Figs. 1 and 2). The connective tissue was moderately increased. No oxyphil cells, no colloid material, no fat cells, no bacteria and no hemosiderin were found. The bloodvessels were moderately congested. There were small hemorrhages in and underneath the capsule, but these might so easily have been the result of handling that they ought hardly be mentioned in this description. Similarly there were areas in which the cells were crowded together apparently because of the pressure of the microtome knife.

In parathyroid (I) there was a ring of round cells encircling one capillary. In parathyroid (II) along one border of fifteen successive sections there was a crescentic area of small round-cell infiltration (Fig. 3). These cells were about twenty-six rows deep and the area occupied about one-twelfth of the periphery of the glandule. In part, these round cells were separated from the epithelial cells by a few strands of connective tissue; in part, the round cells impinged directly upon the parenchyma cells. The nuclei of some of the round cells showed karyorrhexis. Beyond these fifteen sections this round-celled area could no longer be traced. In one gland in particular the perivascular lymph channels were undoubtedly dilated and filled with a granular coagulum (Fig. 4). In this same gland the most striking lesions of our sections were found. These were (Figs. 5 and 6) certain irregular areas occurring near

FIG. 1

FIG. 2

FIG. 1 (× 200) and FIG. 2 (× 312) show each a valve in a vein. All the figures are of sections of the parathyroid gland showing the principal cells (with their deeply-stained nuclei) arranged compactly as is typical for the infant parathyroid and separated into groups and columns by a vascularized connective tissue.

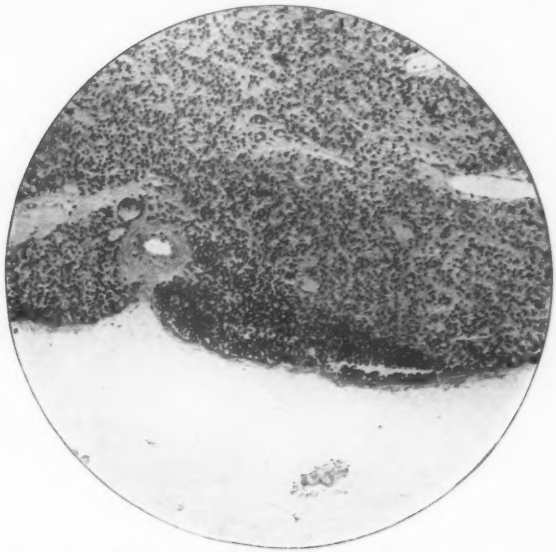

FIG. 3.—In the parathyroid along the border is an area of small round-cell infiltration. × 136.

FIG. 4.—All along the right-hand border of the large vessel is a somewhat sinuous clear channel, a dilated perivascular lymph channel filled with a granular coagulum. Similar dilated lymph channels are seen distributed throughout the section. × 200.

the larger bloodvessels and filled with the same granular material as the perivascular lymph channels. These areas were irregularly rounded or oval, triangular or crescentic in outline, the longest axis about one-fifth of the diameter of the parathyroid. They occurred more frequently at the periphery but sometimes also near the centre of the glandule. In some sections there were two, in some only one, in some no such regions; in one instance an area could be traced by means of its shape and location through sixteen successive sections of 5 microns each. Such an area presented the picture of a clear region, containing a finely granular

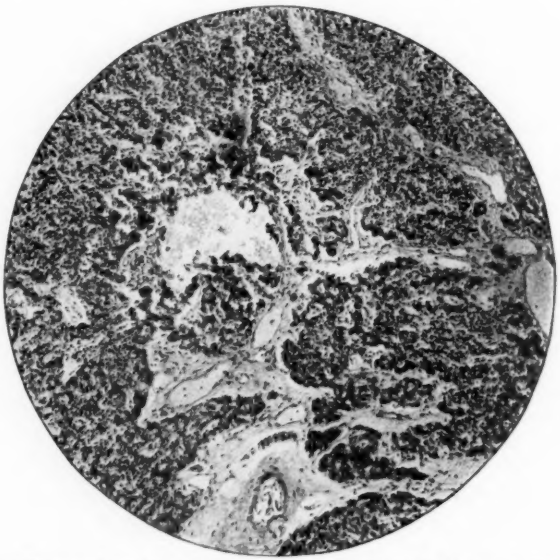

FIG. 5.—Shows an irregular clear area a little above and to the left of the centre. This is filled with the same granular material as is the perivascular lymph channel seen in Fig. 4—interpreted as a ruptured lymph space. × 100.

coagulum with some entirely clear spaces and some detached nuclei and epithelial cells, but with no bacteria and with no red blood cells or pigment. In a few places, a longitudinal section of a capillary could be seen at the edge of the area or traversing it, but never communicating directly with its granular contents. The margins of these regions consisted chiefly of epithelial cells but also in part of bands or strands of connective tissue. The cells of the border projected into the area in the shape of little peninsulas and islets every here and there, and in the neighborhood of the margin seemed crowded together in anastomosing columns separated by narrow clear channels. Such clear channels appeared

to be the extensions of the clear spaces into the surrounding tissue breaking up the compact structure into strands.

Interpretation. Although only four parathyroids were found, and this is the usual number, it is possible that accessory and aberrant glandules escaped detection inasmuch as we did not make serial sections of the whole region in which the parathyroids may occur. In general these parathyroids presented the typical infantile structure with no signs of activity such as are indicated in older subjects by the presence of granular protoplasm, of oxyphil cells, and of acini with colloid. The increase in connective tissue and

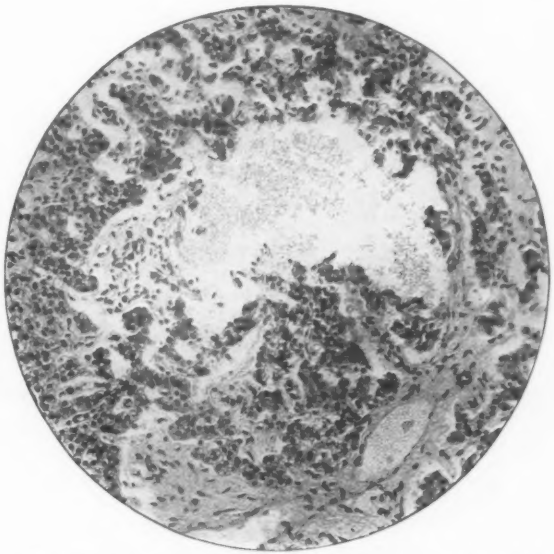

FIG. 6.—The irregular clear area of Fig. 5 much enlarged. It contains a finely granular coagulum with some entirely clear spaces and some detached nuclei and epithelial cells. It extends in the shape of clear channels into the mass of epithelial cells and connective tissue strands surrounding it. × 200.

the congestion are common in parathyroid glands. As to the valves in the veins of the glandules, Yanase considers them a fortunate provision to compensate for the thin walls and great tendency to hemorrhages of the bloodvessels. Yanase found these valves only accidentally and has as yet made no study of their physiological or pathological significance. The round-cell infiltration had evidently no relation to the tetany inasmuch as it was only found in two relatively circumscribed regions. It should be noted that Yanase found numerous round-celled infiltrations in all four parathyroids in a case of pernicious anemia, and Guizzetti inflam-

the larger bloodvessels and filled with the same granular material as the perivascular lymph channels. These areas were irregularly rounded or oval, triangular or crescentic in outline, the longest axis about one-fifth of the diameter of the parathyroid. They occurred more frequently at the periphery but sometimes also near the centre of the glandule. In some sections there were two, in some only one, in some no such regions; in one instance an area could be traced by means of its shape and location through sixteen successive sections of 5 microns each. Such an area presented the picture of a clear region, containing a finely granular

FIG. 5.—Shows an irregular clear area a little above and to the left of the centre. This is filled with the same granular material as is the perivascular lymph channel seen in Fig. 4—interpreted as a ruptured lymph space. × 100.

coagulum with some entirely clear spaces and some detached nuclei and epithelial cells, but with no bacteria and with no red blood cells or pigment. In a few places, a longitudinal section of a capillary could be seen at the edge of the area or traversing it, but never communicating directly with its granular contents. The margins of these regions consisted chiefly of epithelial cells but also in part of bands or strands of connective tissue. The cells of the border projected into the area in the shape of little peninsulas and islets every here and there, and in the neighborhood of the margin seemed crowded together in anastomosing columns separated by narrow clear channels. Such clear channels appeared

to be the extensions of the clear spaces into the surrounding tissue breaking up the compact structure into strands.

Interpretation. Although only four parathyroids were found, and this is the usual number, it is possible that accessory and aberrant glandules escaped detection inasmuch as we did not make serial sections of the whole region in which the parathyroids may occur. In general these parathyroids presented the typical infantile structure with no signs of activity such as are indicated in older subjects by the presence of granular protoplasm, of oxyphil cells, and of acini with colloid. The increase in connective tissue and

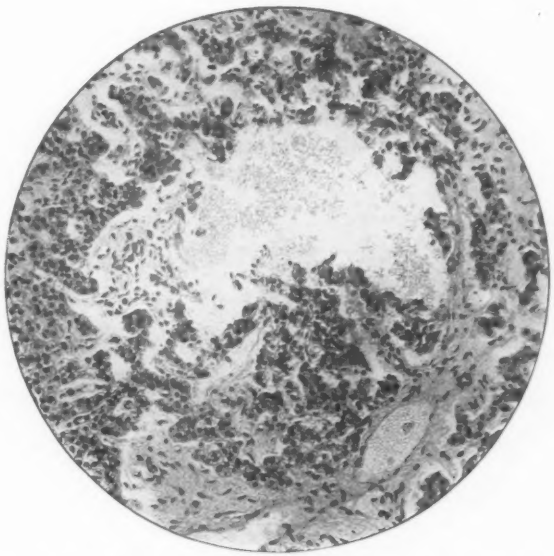

FIG. 6.—The irregular clear area of Fig. 5 much enlarged. It contains a finely granular coagulum with some entirely clear spaces and some detached nuclei and epithelial cells. It extends in the shape of clear channels into the mass of epithelial cells and connective tissue strands surrounding it. × 200.

the congestion are common in parathyroid glands. As to the valves in the veins of the glandules, Yanase considers them a fortunate provision to compensate for the thin walls and great tendency to hemorrhages of the bloodvessels. Yanase found these valves only accidentally and has as yet made no study of their physiological or pathological significance. The round-cell infiltration had evidently no relation to the tetany inasmuch as it was only found in two relatively circumscribed regions. It should be noted that Yanase found numerous round-celled infiltrations in all four parathyroids in a case of pernicious anemia, and Guizzetti inflam-

matory foci of lymphocytes in the parathyroids in two cases of tetanus in adults. The areas which contained the same granular material as the dilated perivascular lymph channels and which occurred in their immediate vicinity are, in our opinion, *ruptured dilated lymph spaces*, or possibly regions of œdema. They were not lined with endothelial cells, but it is known that such lymph spaces bordered by parenchyma cells occur in the liver. These areas were found in the course of a painstaking search for hemorrhages such as have been described by Escherich, Erdheim, and Yanase, and are perhaps the most important pathological finding in the parathyroid glands of our case. We have seen one reference in the literature to similar appearances, but these occurred in two cases of tetanus, not of tetany. Guizzetti describes an extensive œdema and associated lymphatic stasis in one of the four parathyroids from a case of tetanus in a boy, aged eight years. In another case of tetanus in an adult, he found a somewhat similar granular substance around the bloodvessels and also infiltrating the tissue and could not demonstrate that this substance was the residue of an old hemorrhage. As these lesions have not been described before in tetany, and as we found them in only one of the four parathyroids, we think it wiser not to express any opinion as to their significance at present. We do desire to call attention to them and to ask other observers to report whether this condition of lymph stasis or œdema in the parathyroid is a frequent occurrence or an accidental result from some such cause as convulsions.

A very careful search, of course, was made for hemorrhages, "cysts," phagocytes, and pigment, such as have been frequently observed in parathyroids by the Escherich school. None of these were present. In view of the present-day discussion, a negative morphological finding is significant.

If it is somewhat difficult to consider the extensive hemorrhages of Escherich and his school as predisposing causes of tetany, it is still more difficult to consider the less marked lesions described above in our case as important factors in the production of fatal tetany.

My thanks are due Dr. F. S. Mandlebaum, director of the Pathological Laboratory of the Mount Sinai Hospital, for his valuable criticism of this histological study, and to Dr. Koplik for his encouragement in the pursuit of this work.

BIBLIOGRAPHY.

Adler and Thaler. Wien. klin. Woch., 1906, p. 779.
Alquier. Gaz. des Hôp., 1906, lxxix, 1527.
Bell and Hicks. Brit. Med. Jour., 1909, i, 517.
Berger. Med. Klin., 1908, iv, 1604.
Berkeley. Med. and Surg. Rep., Presbyterian Hosp., N. Y., 1906, vii, 170.
Berkeley and Beebe. Jour. Med. Research, 1909, xv, 149.

Biedl. Wien. Klinik, 1903, p. 281.
Bing. Ztschr. f. d. Ges. Physiol. u. Path. d. Stoffwechs., 1908, iii, 11 to 52.
Cautley. Hospital, London, 1908, xliv, 279.
Chvostek. Wien. klin. Woch., 1905, No. 38, p. 969.
Idem. Wien. klin. Woch., 1907, pp. 487, 625, 787.
Cotoni. Rev. de méd., 1909, xxix, 615 to 660.
Edmunds. Lancet, London, 1908, i, 811.
Erdheim. Ztschr. f. Heilkunde, xxv, Abt. f. path. Anat., 1904, v, 1; Mitth. aus den Grenzgeb. der Med. u. Chir., 1906, xvi, 632; Gesell. f. innere Med. u. Kinderheilk., 1906, v, 182; Wien. klin. Woch., 1906, No. 23, 716; Anat. Anzeiger, 1906, xxix, 609.
Escherich. Berl. klin. Woch., 1897, xxxiv, 861; Beibl. z. d. Mitt. d. Gesell. f. Inn. Med. u. Kinderh. in Wien., 1908, vii, 217; Wien. med. Woch., 1908, lviii, 2673 (same as above). Die Tetanie der Kinder (Alfred Hölder), 1909.
Feer. Cor. Bl. f. schweiz. Aerzte Basel, 1908, xxxviii, 713.
Forsyth. Trans. Path. Soc., London, 1907, lviii, 154; Quar. Jour. Med., 1907 and 1908, i, 150 and 287; Jour. Anat. and Physiol., London, 1907 and 1908, xlii, (Third Series II), 141.
Geiss. Ann. Surg. Phil., 1908, xlvii, 523.
Glaserfeld. Berl. klin. Woch., 1909, xlvi (i), 112.
Goris. Jour. de Chir. et Ann. Soc. Belge de Chir., 1905, v, 394.
Guizzetti. Ctblt. f. allg. Path. u. path. Anat., 1907, xviii, 81.
Halsted. Proc. Path. Soc. Phila., 1908, xi, 109.
Harnett. Trans. Path. Soc., London, 1907, lviii, 128.
Hecker. Münch. med. Woch., (1906), 1907, liv, 493.
Hirschberg. Jour. Amer. Med. Assoc., 1908, li, 755.
Humphry. Lancet, 1905, ii, 1390.
Kassowitz. Wien. klin. Woch., 1906, p. 782.
Kirk. Albany Med. Ann., 1908, xxix, 851.
Königstein. Wien. klin. Woch., 1906, pp. 778, 815, 1532.
Krüger. Münch. med. Woch., 1908, lv, 2014.
Leighton. St. Louis Med. Rev., 1908, lvii, 215.
Leopold and Reuss. Wien. klin. Woch., 1908, xxi, 1243.
Lowenthal. Heilkunde, Berl., 1907, xi, 416.
Lundborg. Deut. Ztsch. f. Nervenheil., 1904, xxvii, 217.
MacCallum. Ctblt. f. allg. Path., 1905, xvi, 385; Brit. Med. Jour., 1906, ii, 1282; Proc. Path. Soc. Phila., 1908, xi, 115; also in Ctblt. f. Grenzgebiet.
MacCallum and Voegtlin. Jour. Exp. Med., 1909, xi, 118.
Marinesco. Sem. méd., 1905, p. 289.
Musser and Goodman. Univ. Penn. Med. Bull., 1909, p. 90.
Ochsner and Thompson. The Surgery and Path. of the Parathyroid Glands (C. V. Moseby Publishing Co., St. Louis), 1909.
Ott. Para. Glandules fr. a physiol. and path. Standpoint. Medico-Chirurgical College of Phila., 1909.
Parhon and Urechie. (Revista stiintelor medicale, July and August), 1907, Ref. Münch. med. Woch., 1908, lv (i), 529.
Parhon, Dumitresco, and Nissipesco. Compt.-rend. Soc. de biol., 1909, lxvi, 792.
Pepere. Arch. ital. de biol., Turin, 1907 and 1908, xlviii, 67; Arch. de méd. exp. et d'anat. path., 1908, xx, 21.
Pexa. Klin. therap. Woch., Wien., 1908, xv, 953, 989, 1012, 1053, 1078, 1141, 1178, 1209, 1236; Arch. f. Kinderh., 1910. lv, 1.
Pfeiffer. Mitth. d. Ver. d. Aerzte in Steiermark. Graz., 1909, xlvi, 61 and 97.
Pineles. Sitzungsberichte der Akad. der Wiss. in Wien, 1904, ciii, 199; Mittheil. aus den Grenz. der Med. u. Chir., 1905, xiv, 120; Wien. klin. Woch., 1904, xvii, 517; Wien. klin. Woch., 1906, xix, 691; Deutsches Arch. f. klin. Med., 1906, lxxxv, 491; Jahrb. f. Kinderh., 1907, lxvi, 665; Sitz. d. k. Akad. d. wiss. Math. naturw. Kl. Wien., 1908, cxlvii, 3 Abth., 3 to 8.
Pool. Annals of Surgery, 1907, xlvi, 507.
Pratt. Brit. Med. Jour., 1908, ii, 1680.
Rudinger. Ztschr. f. exp. Path. u. Therap., 1908, v, 205.
Saiz. Wien. klin. Woch., 1908, xxi, 1322; also in Riv. veneta di sc. med. Venezia, xlix, 161.
Sandström. Schmidt's Jahrbücher, 1880, clxxxvii, 114.
Schirmer. Ctblt. f. die Grenzgeb. d. Med. u. Chir., June and July, 1907, x, 401.
Schwartz. Rev. gen. de clin. et de therap., 1907, xxi, 825.
Thiemich. Monatschr. f. Kinderheilk., 1906, v. 165.
Thompson. Amer. Jour. Med. Sci., 1907, cxxxiv, 562.

Thompson and Harris. Jour. Med. Research, 1908, xiv, 135.
Thompson. Ctblt. f. allg. Path. u. path. Anat., 1909, xx, 916.
Vassale and Generali. Rivista di patol. Nerv. e Ment., 1896, i, 95; Arch. ital. de biol., 1896, xxv, 459; ibid., xxvi, 61.
Vassale. Arch. ital. de biol., 1898, xxx, 49.
Von Verebély. Virchow's Archiv., 1907, clxxxvii, 80.
Wassertrilling. Allg. Wiener med. Ztg., 1908, liii, 289, 299, 312.
Weiss. Ueber Tetanie, Volkmann's Sammlung klin. Vorträge, 1881, Nr. 189, 1675.
Welsh. Jour. Anat. and Physiol., 1898, xxxii, 292 and 380.
Yanase. Jahrb. für Kinderheilkunde, lxvii, Ergänzungsheft, 1908, 57.

SARCOMA OF THE VAGINA.

A STATISTICAL STUDY OF 102 CASES, WITH THE REPORT OF A NEW CASE OF THE GRAPE-LIKE SARCOMA OF THE VAGINA IN AN INFANT.

BY JOSEPH MCFARLAND, M.D.,
PROFESSOR OF PATHOLOGY AND BACTERIOLOGY IN THE MEDICO-CHIRURGICAL COLLEGE, PHILADELPHIA.

SARCOMA of the vagina is so rare an affection that the literature contains a total of 101 cases to which I add a new one, making 102 cases upon record. Its rarity and its fatality combine to make it an interesting affection, and when an attempt is made to review the literature of the subject so many features of interest present themselves that the matter becomes quite absorbing.

Sarcoma of the female organs of generation may be divided clinically into those arising from the vulva, from the vagina, from the vesicovaginal septum, from the rectovaginal septum, from the cervix uteri, from the corpus uteri, and from the ovary. In selecting the cases embraced in the statistics given in this paper the attempt has been made to include only those arising from the vagina itself, though in a few the tumors occurred so low down as to be vulvovaginal, and of others the reporters stated that the tumors arose from the vesicovaginal or rectovaginal septa, though their descriptions showed that the tumors corresponded perfectly with vaginal tumors.

The literature begins quite early, in fact, before the separation of the sarcoma and other tumors was made by the microscope, and it is only the opinion of the reviewer, and not absolute knowledge of the tumor tissue that enables him to decide what shall be or shall not be regarded as sarcomas. In working over the case reports a confusion arose through the different methods employed by earlier writers in referring the cases to individuals. Thus, when the literature was reviewed by a clinician he was prone to refer all his collected cases to the clinicians in whose experience

they arose; if, on the other hand, the cases were collected by a pathologist, no attention was paid to this point. The result has been that in a number of the former tabulations and analyses certain cases have been counted more than once. To overcome this difficulty, the method adopted in the present writing has been to credit each case to the author first publishing it regardless of his actual relation to the patient, and to verify every case by referring to the original writing.

Unfortunately the case reports are so commonly imperfect that none of the tabulations can be complete. Thus, the table showing the age incidence contains a confusion of the ages at which the tumor was first observed and the ages at which the patient died. Usually the duration of the case is so brief that not much error results in consequence, but in the case of children it may be important, as in one case in which the tumor is known to have been present at birth, though the child did not die of it until the sixth year.

It is extremely unfortunate that the desire to report a rare case so often leads to its publication before knowledge of it is perfected. The case appears at the clinic, is recoginzed as a rare affection, an ingenious operation is performed, and the patient recovers from it. The clinician then hastens to report the case and tell what has been done without waiting to learn what the final outcome was to be. The evils of this practice are well shown by the tabulation showing the "Fatality of the Different Histological Forms of Sarcoma Vaginæ Exclusive of Sarcoma Botryoides Vaginæ," where out of a total of 58 cases, the termination of the affection is unknown in 34. It is likewise unfortunate that histological examinations have not been made in all cases. The same table shows that no histological data are available in 14 of the cases.

Sarcoma of the vagina occurs at all ages. In our collection of 102 cases there is 1 case in which the tumor was congenital, and 1 that came to operation when eighty-two years of age. It is, however, most frequent in the first, fourth, and sixth decades of life. The occurrence of a special form of infantile sarcoma—sarcoma botryoides, the "grape-like sarcoma"—of which 32 cases are on record, makes it overwhelmingly more frequent in infancy than at any other time of life. Though to all appearances a clinical form of the disease, the sarcoma botryoides vaginæ is so well characterized that throughout most of the following tabulations the tumors have been separated into "miscellaneous" and "botryoides."

The first case of sarcoma botryoides seems to have been recorded by Guersant in 1854; it is, however, difficult to decide what may have been the nature of many other tumors recorded earlier or about the same time as "malignant polypi" of the vagina. A number of such cases were carefully reviewed but rejected and

the policy was adopted of following the example of the earlier compilers who all accept Guersant's case as the first to be reported.

The first careful pathological studies, with special reference to the histology of the tumor came from Kaschewarowa-Rudwena, who curiously enough was able to report two cases from her own clinic, and also observed one in a bitch. Though this tumor differs from the other forms of sarcoma in its clinical manifestations, being characterized by a peculiar papillary or polypoid form with numbers of cysts—the grape-like sarcoma of Pfannenstiel, being observed only in infancy and being highly malignant, it is not so well characterized in all cases as to leave no room for doubt as to its proper classification, and is so varied in histology as not to find a separate place for itself. This is well shown by reference to the table showing the "Histological Forms of Sarcoma Botryoides."

Leaving this peculiar form in a group by itself, we find the remaining sarcomas to form a miscellaneous group embracing nearly all of the histological varieties of sarcoma. The peculiar appearance—grape-like appearance—of sarcoma botryoides has led to much speculation upon its origin. The early age at which the tumor makes its appearance suggests that the tumor is congenital but there is only one case, that of Granicher in which it is certainly known that the tumor was present at birth. Naturally a tumor in such a situation as the vagina might escape observation until it had become of sufficient size to exert pressure symptoms, or as is more usual, until it protrudes from the vulva.

Ahlfeld believed that the peculiar papillary and polypoid character of sarcoma botryoides was sufficient evidence that the tumor arose from the papillæ so numerous in the vaginal wall during the fifth month of intra-uterine life, and believed that all of the tumors were congenital. In this view he was followed by Aubert. Hauser and Kolisko, on the other hand, believe that the tumors are best explained by Cohnheim's theory of "embryonal vestiges," and Kolisko gives the following facts in support of his view: (1) The distribution of the tumor does not correspond with that of the papillæ. (2) The tumors commonly arise from a broad base and as single growths. (3) The tumors of the bladder resulting from extension of the growth are commonly polypoid, though there are never villi in the normal bladder. (4) The recurrent tumors preserve the polypoid character. The occurrence of a warty vaginal mucosa such as is described by Soltmann and was found in one of Kolisko's own cases can be attributed to the greater ease with which the tumor spreads in the mucosa as contrasted with the subjacent muscular tissue. (5) The structure with its miscellany of round and spindle cells, giant cells, muscle cells, epithelial cells, and cartilage, is in favor of Cohnheim's theory. Still another view of the etiology of the tumor has been suggested by Pfannenstiel,

that is, that it arises from the endothelium of the blood and lymph capillaries.

The clinical course of the sarcoma botryoides is much the same in all cases. The tumor first calls attention to itself either by projecting through the vulvar orifice or through the occurrence of a bloody discharge from the vagina. In most cases the diagnosis of "vaginal polyp" is made and the growth excised or divulsed. In most cases the tumor quickly recurs, after which there may be a succession of operations or a radical operation. In one case in which the operation was so radical that the entire vagina, uterus, tubes, and ovaries were removed the little patient is said to have recovered. In all other cases the tumor recurred, became inoperable, distended the vagina so as to fill the pelvis, invaded the bladder and caused the death of the patient either through exhaustion or from uremic blood poisoning. In no case has the tumor given metastasis. It is a purely local progressively extending tumor.

When the reports of other infantile sarcomas are read we find that they parallel the clinical course of sarcoma botryoides except that they lack the grape-like appearances, are not polypoid and not cystic.

The clinical course of the adult sarcomas is in general much the same. Though coming more early to operation, they, with the exception of the more benign forms, tend to rapid recurrence, to infiltrate the bladder and to cause a fatal termination through interference with the urinary passages. In these cases metastasis is very rare; the disease is local.

The geographical distribution of the tumor though shown in one of the tables is of small interest. The tumor attracted most attention in Germany, has been made the subject of numerous communications, and it is safe to surmise that few cases have escaped publication in that country. This gives Germany an apparent preponderance of cases.

The chronological distribution though more accurate is subject to the error that arises from evanescent interest in the subject. My tabulation is based chiefly upon the date of publication, but is inaccurate, because when interest upon the subject was aroused, cases from years before were sometimes hurried into print. The table shows, however, that the sarcoma botryoides averages one case each year and eight months; the miscellaneous vaginal sarcomas, one case each year and six months.

Certain writings on the subject, of special merit both from the scientific and synoptical points of view, should receive mention. The best of these are:

Veit. Handbuch der Gynäkologie, 1897, i, 354.
Powers. St. Bartholomew's Hospital Reports, xxxi, 1895.
Kolisko. Wiener klin. Wochenschrift, 1889, pp. 109, 130, 159.
Williams. Twentieth Century Practice of Medicine, 1898, xvii, 530.
Jellett and Earl. Trans. Royal Acad. of Med. of Ireland, xxii, 1904.

A word should be said with reference to the sarcomas that arise from the vesicovaginal and rectovaginal septæ. Being more deeply situated than the vaginal mucosa from which the true vaginal sarcomas arise, their tendency is to invade the deeper tissues, fill up the pelvis and give metastases to the pelvic and abdominal lymphatics and not to confine themselves to the vagina and bladder.

Sarcoma Botryoides Vaginæ—New Case. F. E. was born March 22, 1908, of parents in whose family history and in whose personal histories there seemed to be nothing of interest so far as the present circumstances are concerned. They were already possessed of one healthy child, and since the death of the one whose case we are about to consider, have became the parents of another.

On July 6, 1908, Dr. Robert L. Pitfield, of Germantown, was called to see the child, then aged three and one-half months, and shown a small tumor first observed by the nurse two days before. Two days later, at his request, we saw the little patient together and carefully examined the tumor, which proved to be peculiar and interesting.

FIG. 1.—Photograph showing the tumor projecting from the vulva when the patient cried and made expulsive efforts. This photograph was made shortly before the patient's death by Dr. George E. Pfahler.

When the thighs of the baby were separated, the vulvar orifice gaped slightly and permitted a laterally compressed reddish body of small size and moist appearance to be seen (Fig. 1). When the labia were more widely separated for a better view of the formation, the child began to cry and make expulsive efforts which resulted in the descent through the vulvar orifice of an irregularly hemispherical tumor about 3 cm. in its greatest diameter that sprang from the posterior and left lateral walls of the vagina. It was red in color and at first sight appeared smooth. This appearance was later found to depend upon the presence of considerable mucopus with which the surface was bathed, for when it was wiped off so that a more careful examination could be made, the growth

was found to be composed of a polypoid mass, the intervals between the polypi being filled with the secretion and so disguised. Upon the surface of the tumor a number of small, clear, amber-colored cysts were conspicuous when the secretion was wiped off. The largest of the cysts was about 0.5 cm. in diameter. They gave the growth much the appearance of a bunch of currants infiltrated with reddish-gray slime.

When the child ceased to cry the tumor again retracted into the vagina. Dr. Pitfield had already made the diagnosis of "grape-like sarcoma," which I confirmed, though we were uncertain whether the growth originated in the vagina where we saw it or whether it sprang from the cervix uteri.

A very unfavorable prognosis was at once rendered, with the recommendation that an operation be immediately arranged for.

Some days later the child was taken ill with enterocolitis, and as at that time it was very warm and sultry in Philadelphia, it was taken to Ocean City, N. J. Here the patient was treated by Dr. Howard Reed, and speedily convalesced from the summer complaint. Upon July 24, Dr. Reed was able to operate and removed as much of the tumor as was attached to the vaginal wall. This mass, which was sent to me in formaldehyde solution, formed the foundation of my studies of the histological character of the tumor.

The child improved rapidly after the operation, but the wound did not heal and the tumor recurred so rapidly that on August 28 it was necessary to perform a second excision. In ten days the tumor had again recurred and grew so rapidly that it soon filled the entire vagina. The patient was now seen in consultation by Professor W. E. Ashton, who declared the condition to be inoperable. It was, therefore, thought that the *x*-rays might hold out a chance of benefit and the little patient was taken for the purpose to Dr. George E. Pfahler who began with three treatments weekly. The early results appeared encouraging. After six treatments the tumor had diminished to one-third of its original size, and after ten treatments to about one-fourth. An inguinal enlargement entirely disappeared. The baby was, however, much troubled with the summer diarrhœa and became very feeble. Partly because of the patient's general condition, and partly because he was to leave the city for a short time, Dr. Pfahler discontinued the treatments for a month. During that time, in spite of progressive emaciation and continued diarrhœa, the tumor grew again to its original size.

The condition of the little patient in the meantime became very distressing because of increasing difficulty of micturition and defecation. This difficulty increased to such an extent that the violent expulsive efforts of the patient had to be supplemented by com-

pression of the lower part of the abdomen by the mother or nurse in order that a small quantity of urine or feces could be discharged.

These conditions persisted and increased. The child suffered almost continuously, slept scarcely at all, emaciated almost to a skeleton, and died December 8, 1908, aged eight and one-half months, the tumor having been known to exist for just five months.

Autopsy. December 9, 1908. The body is that of a much-emaciated female infant. Rigor mortis marked. Thorax, abdomen, and left arm livid. Occasional petechia upon the skin.

From the vaginal orifice there projects a pyriform, dark colored, necrotic mass measuring about 1.5 by 2 cm. This can be traced into the vagina to a broad attachment upon the left lateral and posterior walls. Upon the surface a few small opalescent cysts (?) can be seen.

The appearance of the tumor is now very different from that first noted in the living child. Its grayish-red color is now changed to a dark necrotic red-black; its polypoid character has disappeared and it forms a solid mass. The clear cysts, like currants, that formed a large part of the original growth are gone and in their place are a few cysts with semiopaque contents. In addition to the chief mass there are a few pinhead sized nodules on the right labium majus, and a nodule the size of a pea in the vestibule.

The body was opened by the usual incisions, the nervous system not being removed.

Thorax: Pericardium, normal. Pleuræ, normal. Heart, normal —moderator band in the left ventricle. Right lung, hypostatic congestion. Left lung, hypostatic congestion; scattered foci of atelectasis. Thoracic lymph nodes somewhat larger and redder than is usual in infancy but otherwise normal. No thoracic metastases.

Abdomen: Spleen, large, bluish-purple, mottled. Upon section congested but otherwise normal. A small supernumerary spleen in the gastrosplenic omentum. Adrenals, normal. Liver, normal. Bile ducts, normal. Gall-bladder, normal. Duodenum, normal. Stomach, dilated. Small intestine, enlargement of the lymph follicles. Large intestine, enlargement of the lymph follicles. Mesenteric lymph nodes, slightly enlarged and red like those of the thorax. No signs of abdominal metastases. Kidneys, hydronephrosis and dilated ureters on both sides. The kidney substance also showed a mild grade of parenchymatous degeneration.

Pelvis: The pelvic cavity is completely filled by a mass formed by adhesion of all of the viscera. The chief mass is found to be the tumor distending the vagina. This tumor is dark red, almost black in color and forms a mass measuring 4.5 cm. in length by 3 cm. in breadth. It springs by a broad attachment from the posterior and left lateral walls about 1.5 cm. from the cervico-vaginal junction. The growth is lobulated and its surface generally

warty but highly necrotic. The anterior vaginal wall is invaded in its central third by an aggregation of wart-like formations most of which are sessile, though some are pedunculated. The vaginal wall at the attachment of the tumor is considerably thickened, and appears to be infiltrated around the base of the neoplasm; the remainder is thin and attenuated. At no point has the tumor broken through the vaginal wall except at its base. The right anterior vaginal wall is attached to the bladder by easily dissected adhesions, but on the left side the walls of the two viscera are so infiltrated by the neoplasm as to form a continuous mass.

Upon opening the bladder its wall is found to be infiltrated; and a mass of neoplasm about 2 cm. in diameter springs from the left anterior wall, occupies the entire trigone, and projects into the interior. Through the centre of this mass there is a ragged opening which connects with the urethra below. The bladder contains about 75 c.c. of turbid urine. The tumor mass in the bladder is entirely different in appearance from the vaginal mass, being grayish-pink in color. It is devoid of the hemorrhagic character of the vaginal growth. It is soft and œdematous. The surface is smooth and the substance translucent.

The uterus is very small and is peculiarly divided by a transverse cicatricial band so that the cervix and corpus are almost separated one from the other. The corpus also has a peculiar angulation and twist in consequence of the pressure of the band. The uterus is adherent to the bladder anteriorly and to the rectum posteriorly. It is, however, easily dissected free and is in no way invaded by the tumor. The vaginal portion of the cervix is slightly eroded, but it and the uterine mucosa are free of warts or polyps.

The rectum is so compressed as to be like a ribbon in appearance. It is empty and is not invaded by the tumor.

Both ureters were dissected and traced from the bladder to the kidneys. Their dilatation and the hydronephrosis does not depend upon obstruction of their vesical orifices, but is due to the regurgitation of urine during the efforts made to expel the urine from the bladder.

The right ovary and tube are in fairly normal condition.

The left ovary and tube are caught in a mass of adhesions and were not found in the dissection.

The tumor grew by continuous extension and infiltration; there were no lymphatic metastases in the pelvis.

The terminal sufferings of the patient were made clear by the cystic mass that obstructed the urethra and caused the backward flow of the urine into the ureters and pelves of the kidneys, and by the distended vagina which compressed the rectum almost to complete obstruction.

Death was probably caused by uremic blood poisoning following the damage to the kidneys, though it could be sufficiently explained by the exhaustion of the little patient through efforts to overcome

the mechanical impediments to urination and defecation. No signs of anything in the right groin to correspond to the mass that disappeared under the use of the *x*-ray could be found.

The original appearance of the tumor, with its polypoid cysts, like a "bunch of currants," its malignancy, the age of the little patient, and the clinical course seem to leave no doubt that the case belonged to the rare neoplasms to which Pfannenstiel first applied the term "*grape-like sarcomas*," and which are now frequently known as *sarcoma botryoides vaginæ*.

Histological Examination of the Tumor. The first tissue subjected to microscopic examination was that removed at the first operation by Dr. Reed. It is, indeed, the only tissue whose study has been of much use. Undue eagerness to preserve the entire pelvic viscera for the museum caused us to neglect to secure fragments for histological study, and when it became desirable to do so it was too late, as the reagents to which they had been subjected had destroyed their cellular structure (Figs. 2, 3, and 4).

The portion studied, therefore, corresponds to that examined by Dr. Pitfield, and myself, at our consultation of July 8, 1908, and consists of an irregularly hemispherical fragment. The flattened surface being that through which the cutting instrument passed; the rounded surface that of the tumor itself. Examination of this fragment shows that although it was removed little more than two weeks after it had been examined *in situ* it had undergone some change. It appears less lobulated and no longer contained the numerous cysts. Such cysts as are present appear smaller, and after immersion in the formaldehyde quite inconspicuous.

The sections cut for examination with the microscope were made in a direction perpendicular to the surface and passed through the entire thickness of the excised fragment.

The surface was, in general, covered with the vaginal squamous epithelium. This was more or less densely infiltrated with leukocytes, by which it was more or less completely disorganized in scattered areas. The destruction of the epithelium was almost confined to the exposed surface; where it dipped down between the papillary formations it was fairly well preserved. The leukocytic invasion was most marked upon the surface but occasionally penetrated to a considerable depth into the tissue of the tumor proper.

The tumor tissue began immediately beneath the vaginal epithelium, and in many places the superficial portion of the growth was a confused aggregation of dissociated epithelium, leukocytes, cells of the tumor proper, and cells that may have belonged to the fibromuscular tissues of the vaginal wall.

The more superficial portion of the tumor tissue differed from its deeper portions in a peculiar wide separation of the cellular elements ascribable to œdema. This œdema seemed to reach its maximum at occasional foci near the surface which appear to correspond to the

cysts. If such were the case, one was much deceived, for the cystic appearance was striking. However, the microscopic study of the tissues revealed the presence of no true cysts. This explanation of

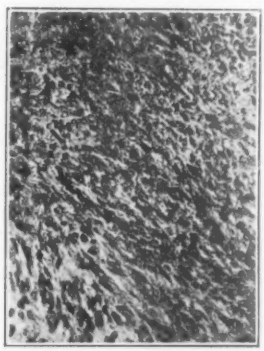

FIG. 2

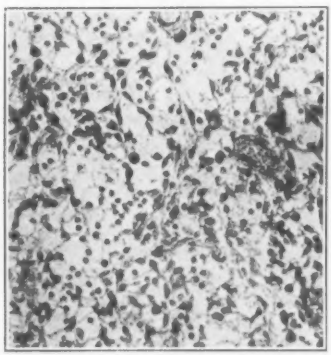

FIG. 3

FIG. 2.—Photomicrograph showing the generally degenerated character of the tumor tissue, but still showing its structure to be composed of spindle-cells.

FIG. 3.—Photomicrograph of one of the œdematous areas of the tumor tissue.

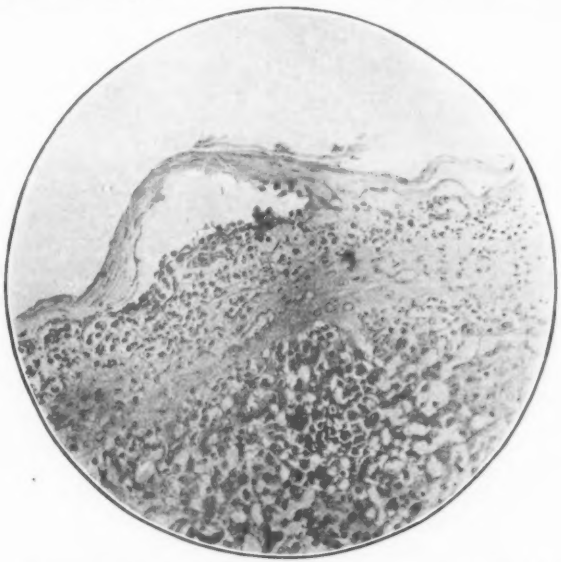

FIG. 4.—Photomicrograph showing the surface of the tumor. The vaginal epithelium, by which the tumor is covered, is found to be fairly well preserved at this point, though it is separated and elevated at the centre, because of an extensive infiltration of leukocytes. Immediately below the epithelium the tumor tissue begins in a somewhat œdematous and miscellaneous collection of cells.

œdematous tumor villi and polypi simulating cysts is quite in keeping with the subsequent changes in its structure, for it appeared highly cystic when first seen, less so when Dr. Reed operated upon it, and scarcely at all so when it was finally examined at autopsy. In thus explaining the cystic appearances I am supported by the observation of Kolisko who, in speaking of the cyst-like formations in one of the tumors examined by him, says that "they were not actual spaces, but points at which the cells were widely separated from one another by fluid." It is a pity that we did not think to puncture one or two of them at the first examination, yet it is doubtful whether even such treatment would have made us sure of their nature, as the œdematous fluid would probably have leaked out much like the fluid from a punctured cyst.

The tissue of the tumor proper is almost entirely composed of spindle cells. They are somewhat irregular in shape and differ materially in different parts of the tumor. In what may be regarded as its "healthy" parts the cells are fairly regular in shape and form definite short spindles which lie side by side in fasciculi. Here and there one finds a strand of fibrillar tissue, but usually only in proximity to small bloodvessels. Here and there in the denser parts of the cellular growth small bloodvessels with only the endothelial coat may be found.

From such "healthy" and dense portions the tissue passes by imperceptible stages into the œdematous portions first described, where the cells are widely separated one from another and form a miscellany of spindle, stellate, clavate, and irregularly rounded cells. Among these are many leukocytes and not a few plasma cells. The nuclear structure is, in general, badly preserved. The formaldehyde fixation is imperfect, but only a small part of the appearance can be referred to it, as karyokinetic figures are numerous in the better preserved tissue areas, and though epithelial cells and leukocytes stain well, the nuclei of tumor cells in juxtaposition to them stain uniformly and palely. Again, in the poorly preserved portion of the tumor tissue and in the œdematous portions, though the nuclei of the leukocytes, cells of the bloodvessels, and those of a few of the tumor cells stain well, the generality of the tumor cells show more or less karyolysis and swelling to many times the normal size. Among the monstrous cells thus formed many have nuclei of giant size, and a few have several nuclei. These small giant cells are, however, too small and too few to merit much attention or affect the nomenclature of the tumor.

Although many sections were examined with care, no muscle cells other than could be accounted for by proximity to vessels, or be looked upon as remnants of the original vaginal tissue could be found. It was quite clear that neither muscle or cartilage were true components of the tumor.

The tumor, therefore, appears to be a simple *spindle-cell sarcoma* with localized foci of œdema and degeneration.

In the excised fragment only the epithelial coat of the vagina and the tumor tissue were present. It seemed clear that the tumor had grown in the mucosa, elevated the epithelium, and dissected it from the muscle.

Table Showing the Chronological Distribution of Cases of Sarcoma of the Vagina (not including Sarcoma Botryoides).

1867.	1 case.	Ahlfeld.
1869.	1 case.	Meadows.
1869.	1 case.	Heckford. Infant.
1872.	2 cases.	Spiegelberg.
1872.	2 cases.	Kaschewarowa-Rudwena.
1875.	1 case.	Fränkel.
1875.	1 case.	Mann.
1880.	1 case.	Biardi.
1884.	1 case.	Simmons.
1885.	1 case.	Mentzel.
1885.	1 case.	Underhill.
1885.	1 case.	Young.
1886.	1 case.	Gervis.
1886.	1 case.	Handfield-Jones.
1887.	1 case.	Parona.
1887.	1 case.	Spadaro.
1888.	1 case.	Steinthal.
1889.	1 case.	Herzfeld.
1889.	1 case.	von Rosthorn.
1889.	1 case.	Marshall. Infant.
1890.	1 case.	Odebrecht.
1891.	1 case.	Alglave and Mibian.
1891.	1 case.	Ferrari.
1891.	1 case.	Gow.
1891.	1 case.	Hofmokle.
1891.	1 case.	Kalustow.
1891.	1 case.	Wirtz.
1892.	1 case.	Gatti.
1892.	2 cases.	Oliver.
1892.	1 case.	Wirt.
1893.	1 case.	Tor Neumann.
1894.	1 case.	Klein.
1894.	1 case.	Merutz.
1895.	1 case.	Senn.
1896.	2 cases.	Horn.
1896.	1 case.	Rubeska.
1897.	1 case.	Amann.
1898.	1 case.	Morestin.
1898.	1 case.	Fräncke.
1899.	1 case.	Gebhardt.
1899.	2 cases.	Jung.
1899.	1 case.	Smallwood-Savage.
1899.	1 case.	Waldstein. Infant.
1899.	1 case.	Strassmann. Infant.
1900.	1 case.	Moovis.
1900.	1 case.	Seitz.
1901.	1 case.	Piechand and Guyot. Infant.
1902.	1 case.	Macnaughton-Jones.
1903.	1 case.	Rashkes.
1904.	1 case.	Jellett and Farl.
1904.	1 case.	Marullez. Infant.
1905.	1 case.	Rollin.
1905.	1 case.	Peyroche. Infant.
1906.	1 case.	Boldt.
1906.	1 case.	Potherat.
1907.	1 case.	Jellett.
1907.	1 case.	Holmes. Infant.
1907.	1 case.	Amann. Infant.
1908.	1 case.	Moovis.
1908.	1 case.	Rosenberger.
1908.	1 case.	Deck. Infant.
1909.	1 case.	Favill.
1909.	1 case.	McLean.

Total { Adult 58, Infantile 10

68 cases in 42 years.

Table Showing the Chronological Distribution of Cases of the Grape-like Form of Sarcoma of the Vagina or Sarcoma Botryoides Vaginæ.

1854.	1 case.	Guersant.
1874.	1 case.	Marsh.
1880.	1 case.	Ahlfeld.
1880.	1 case.	Sänger.
1881.	1 case.	Soltmann.
1882.	1 case.	Hauser.
1883.	1 case.	Babes.
1883.	1 case.	Smith.
1888.	2 cases.	Fricke.
1888.	1 case.	Gränicher.
1888.	1 case.	Kövner.
1888.	1 case.	Schustler.
1888.	1 case.	Steinthal.
1889.	3 cases.	Kolisko.
1895.	2 cases.	Powers.
1896.	1 case.	Braun.
1896.	1 case.	Hollander.
1900.	1 case.	Lea.
1900.	1 case.	Starfinger.
1900.	1 case.	Brown.
1902.	1 case.	Rabe.
1903.	1 case.	Wrede.
1904.	1 case.	Le Dentu.
1905.	1 case.	Aubert.
1907.	1 case.	Kelly and Noble.
1907.	1 case.	Rosenbach.
1909.	1 case.	Schiller.
1910.	1 case.	Miller and Gurd.
1910.	1 case.	Knoop.
1911.	1 case.	McFarland.

Total: 34 cases in 57 years.

Table Showing the Anatomical Origin of Sarcoma Vaginæ, not Including Sarcoma Botryoides.

	Cases
Vulvovaginal entrance	2
Entire circumference of the vagina	2
Anterior wall	20
Posterior wall	19
Right wall	2
Left wall	4
Vesicovaginal septum	1
Rectovaginal septum	1
Not stated	17
	68

Table Showing the Anatomical Origin of Sarcoma Botryoides Vaginæ.

	Cases.
Vulvovaginal entrance	2
Whole vagina	2
Anterior wall	10
Posterior wall	4
Right wall	2
Left wall	4
Not stated	10
	34

Table Showing the Geographical Distribution of the Reported Cases of Sarcoma Vaginæ, not Including Sarcoma Botryoides.

	Cases.
Germany	27
France	6
Italy	5
United States	5
British Isles	20
Austro-Hungary	4
Russia	1
Switzerland	1
	69

Table Showing the Geographical Distribution of the Reported Cases of Sarcoma Botryoides Vaginæ.

	Cases.
Germany	21
Switzerland	1
United States	5
France	3
British Isles	4
	34

Table Showing the Fatality of the Different Histological Forms of Sarcoma of the Vaginæ Exclusive of Sarcoma Botryoides Vaginæ.

Histological character of the tumor.	D.	R.	Termination unknown.	Cases.
Round-cell sarcoma	0	1	8	9
Spindle-cell sarcoma (this includes Horn's case called alveolar spindle-cell sarcoma with much pigmentation)	5	3	9	17
Round- and spindle-cell sarcoma (this includes von Rosthorn's case in which Veit states that there were giant cells)	2	0	0	2
Myosarcoma (this includes all forms in which muscle cells were found)	0	0	2	2
Fibrosarcoma (this includes Ahlfeld's case called sarcoma fibrosum multo-et-fuso-cellulare telangiectoides diffusum)	1	2	0	3
Myxosarcoma	0	2	0	2
Melanosarcoma	1	0	1	2
Giant-cell sarcoma	0	0	1	1
Angiosarcoma (this includes Kalustow's case called sarcoma telangiectoides seu angio-matosum hemorrhagicum)	2	0	1	3
Endothelioma (this includes Klein's case called lymph-angio-endothelioma cavernosum hemorrhagicum)	0	0	3	3
Unknown	5	0	9	14
	16	8	34	58

Table Showing the Fatality of the Different Histological Forms of Sarcoma Botryoides Vaginæ.

Histological character of the tumor	D.	R.	Termination unknown.	Cases.
Round-cell sarcoma	1	0	0	1
Spindle-cell sarcoma	3	0	1	4
Round- and spindle-cell sarcoma	5	1*	0	6
Myosarcoma (includes all cases in which muscle cells were found)	3	0	0	3
Myo-fibro-sarcoma	1	0	0	1
Fibrosarcoma	2	0	1	3
Myxosarcoma	1	0	0	1
Unknown	10	1†	4	15
	26	2	6	34

* No return in 3 years.
† Was under observation only two months.

Table Showing Age Incidence, Histological Character, and Termination of Reported Cases of Grape-like Sarcoma of Infancy or Sarcoma Botryoides Vaginæ.

Age of patient.	Cases.	Nature of the tumor.	Termination.
Not given	1	?	?
Congenital	1	?	Died.
3 months	1	Spindle-cell sarcoma	Died.
6 months	1	Spindle-cell sarcoma	Died (of bronchopneumonia).
6 months	1	Round- and spindle-cell sarcoma	Died.
7 months	1	Round- and spindle-cell sarcoma	Died.
8 months	1	?	Died.
9 months	1	?	No return in two months.
12 months	1	Myosarcoma	Died.
18 months	1	?	Died.
18 months	1	Myofibrosarcoma	Died.
18 months	1	Round- and spindle-cell sarcoma	Died.
18 months	1	Spindle-cell sarcoma	Died.
21 months	1	?	Died.
24 months	1	?	Died.
24 months	1	?	?
24 months	1	Myxosarcoma	Died.
28 months	1	Fibrosarcoma	Died.
28 months	1	Myosarcoma	Died.
30 months	1	Round- and spindle-cell sarcoma	Recovered(no return in 3 years).
30 months	1	?	Died.
30 months	1	?	Died.
30 months	1	Fibrosarcoma	?
30 months	1	?	Died.
32 months	1	?	?
36 months	1	Spindle-cell sarcoma	?
36 months	1	?	Died.
36 months	1	Small round-cell sarcoma	Died.
40 months	1	Fibrosarcoma	Died.
42 months	1	Myosarcoma	Died.
44 months	1	?	Died.
48 months	1	?	?
53 months	1	Round- and spindle-cell sarcoma	Died.
60 months	1	Round- and spindle-cell sarcoma	Died.
	34		

Table Showing Age Incidence, Variety, and Termination of Cases of Miscellaneous Sarcoma of the Vagina, not Including Sarcoma Botryoides.

Age of patient.	Cases.	Nature of tumor.	Termination.
8 months	1	Myxosarcoma	Died (of scarlatina while in the hospital).
10 months	1	?	Died.
11 months	1	Rhabdomyosarcoma	Died.
16 months	1	Perithelioma	Recovered.
17 months	1	Round-cell sarcoma	Died.
18 months	1	?	Died from peritonitis from accident to operation wound.
18 months	1	?	?
18 months	1	Endothelioma	Died.
24 months	1	Myosarcoma	Died.
31 months	1	?	Died.
14 years	1	Endothelioma	?
15 years	1	Sarcoma fibrosum multo-et fusocellulure telangiectodes hemorhagium. (In our tables this is classed as fibrosarcoma.)	Died.
15 months	1	Spindle-cell sarcoma	Died.
15 years	1	Rhabdomyosarcoma	?
16 years	1	Round-cell sarcoma	Recovered.

Table Showing Age Incidence, Variety, and Termination of Cases of Miscellaneous Sarcoma of the Vagina, not Including Sarcoma Botyroides (Continued).

Age of patient.	Cases.	Nature of tumor.	Termination.
17 years	1	Spindle-cell sarcoma	Died.
17 years	1	Spindle-cell sarcoma	Died.
17 years	1	Spindle-cell sarcoma	?
19 years	1	?	Died.
23 years	1	Sarcoma telangiectoides seu angioma hemorrhagicum. (In our tables this is classed as angiosarcoma.)	Died.
25 years	1	Round-cell sarcoma	Died.
25 years	1	Round-cell sarcoma	?
28 years	1	?	?
28 years	1	Spindle-cell sarcoma	Discharged
30 years	1	Round-cell sarcoma	?
30 years	1	Myxosarcoma (myxoma?)	Recovered.
31 years	1	Melanotic spindle-cell sarcoma	Died.
32 years	1	Angiosarcoma	Died.
32 years	1	?	?
33 years	1	Small round-cell sarcoma	?
34 years	1	Spindle-cell sarcoma	?
34 years	1	?	Discharged in 6 weeks
34 years	1	Small round- and spindle-cell sarcoma	?
35 years	1	Fibrosarcoma	Recovered.
35 years	1	?	Died.
35 years	1	Spindle-cell sarcoma	Recovered.
37 years	1	Melanotic sarcoma	?
38 years	1	Spindle-cell sarcoma	?
39 years	1	Endothelioma	?
39 years	1	?	?
41 years	1	Spindle-cell sarcoma	Recovered
43 years	1	Round- and spindle-cell sarcoma with giant cells. (In our tables this is classed as a round- and spindle-cell sarcoma.)	?
44 years	1	Spindle-cell sarcoma	?
49 years	1	Spindle- and stellate-cell sarcoma with muscle cells. (In our tables this is classed as a myosarcoma.)	?
49 years	1	Alveolar spindle-cell sarcoma	Died.
50 years	1	Round- and spindle-cell sarcoma	Died.
51 years	1	?	Died.
54 years	1	Sarcoma, hypernephroma or lymphangioma hypertrophicum (In our tables we class this as histologically unknown.)	?
55 years	1	Angiosarcoma or endothelioma	Recurred
55 years	1	?	?
55 years	1	Spindle-cell sarcoma	Recovered
56 years	1	Lymphangio-endothelioma cavernosum hemorrhagicum. (In our tables we class this as endothelioma.)	?
58 years	1	?	Died.
58 years	1	Small round-cell sarcoma	?
60 years	1	Round- and oat-shaped-cell sarcoma	Died.
70 years	1	?	?
82 years	1	Spindle-cell sarcoma	Recovered.
Unknown	11		
	68		

Age Incidence of Sarcoma of the Vagina.

	Miscellaneous.	Botryoides.
First decade	10	34
Second decade	9	0
Third decade	5	0
Fourth decade	16	0
Fifth decade	5	0
Sixth decade	9	0
Seventh decade	1	0
Eighth decade	1	0
Ninth decade	1	0
	57	34
"Young woman"	1	
"Old maid"	1	
Age not given	9	
	68 miscellaneous	
	34 botryoides	
	102 cases	

Reported Cases of Sarcoma of the Vagina.

I. Infantile. *Grape-like Sarcoma or Sarcoma Botryoides.*

1. Ahlfeld, I. F. Archiv. f. Gynäkologie, 1880, xvi, 135.
2. Aubert, L. H. Revue médicale de la Suisse Romande, 1905, xxv, 584.
3. Babes, V. von Ziemssen's Handbuch der spezielle Path. u. Therapie, 1883 and 1884, xiv, 475.

Billroth. Chirurg. Klinik, 1871. This case is reported by Kolisko (see below), and is accredited to him.

4. Braun. Inaugural Dissertation. Greifswald, 1896.
5. Brown, B. B. Baltimore Gynecological Society, 1900.

Demme. Med. Bericht ueber die Thätigkeit der Jennerschen Kinderspitals in Bern, 1892, p. 95. This is an amplification of the facts about the case published by Gränicher (see below).

6. Le Dentu. La Presse Médicale, 1904, xi, 321.
7, 8. Frick, C. Inaugural Dissertation. Halle a/s, 1888; Virchow's Archives, 1889, cxvii, 284. Reports two cases: (1) From the clinic of Professor Roosenberg in Haag; (2) from the clinic of Professor von Volkmann in Halle a/s.
9. Gränicher. Inaugural Dissertation. München, 1888. This case occurred in the clinic of Professor Demme.
10. Guersant, M. P. Moniteur des Hôpitaux, 1854, p. 18.
11. Hauser. G. Virchow's Archives, 1882, lxxxviii, 165.
12. Holländer. Zeitschrift für Geburtshülfe und Gynäkologie, 1896, xxxiv, 125.
13. Kelly and Noble. Gynecology and Abdominal Surgery, 1907, i, 820.
14, 15, 16. Kolisko. Wiener klinische Wochenschrift 1889, 109 *et seq.* Reports 3 cases: (1) Child named Tredham from Professor Weinlechner's clinic; (2) child named Floh from Professor Weinlechner's clinic; (3) child named Heindle from Professor Billroth's clinic.
17. Körner. Inaugural Dissertation. Halle a/s, 1888.
18. Knoop. Zeitschrift für Geburtshülfe und Gynäkologie, 1910, lxvi, No. 3, 569.
19. Lea, A. W. W. Obstetrical Transactions, London, 1900, xlii, 143.
20. Marsh. Transactions of the Pathological Society of London, 1874, xxv, 178.
21. McFarland, Joseph. Present Contribution.
22. Miller and Gurd. Surgery, Gynecology, and Obstetrics, October, 1910, xi, No. 4, 391.
23. Powers, D'Arcy. St. Bartholomew's Hospital Reports, 1895, xxxi, 121; also Trans. of the Pathological Society of London, October 15, 1895; also British Medical Journal, 1895, ii, 973.
24. Powers, D'Arcy. An old specimen No. 3030 from the Museum of St. Bartholomew's Hospital. See the Hospital Reports, 1895. xxxi, 121.

25. Rabé. Archiv. de méd. des enfants, 1902, v, 584; also Revue de Gynecologie et de Chirurgie Abdominale, 1903, vii, 941.

Rollin. Revue de Gynecologie et de Chirurgie Abdominale, 1906, x, 3. This is the case previously reported by Le Dentu (see above).

26. Rosenbach, L. Charité Annalen, 1907, xxxii, 393.

27. Sänger, M. Archiv. f. Gynäkologie, 1880, xvi, 58.

28. Schiller. Monatschrift f. Geburtshülfe u. Gynäkologie, April, 1909.

Schuchardt. Verhandlung der deutschen Gesellschaft für Gynäkologie, 1888, 239. He reports the same two cases that form the basis of the Inaugural Dissertation by Fricke. (1) From the clinic of Professor Roosenberg in Haag; (2) from the clinic of Professor von Volkmann in Halle a/s.

29. Schustler, M. Wiener klinische Wochenschrift, 1888, i, 148; also Verhandlung ärztlicher Gesellschaften und Vereine, May 14, 1888.

30. Smith. American Journal of Obstetrics, 1883, xvi, 555, with a supplementary note, in the same journal, 1893, xxvii, 577.

31. Soltman, O. Jahrbuch für Kinderheilkunde, 1881, xvi, 418.

32. Starfinger, E. Inaugural Dissertation, Berlin, 1900.

33. Steinthal, C. F. Virchow's Archives, 1888, cxi, 449.

Thomas. A case given by Powers (see above) seems to be vulvar and not vaginal. According to Peyrache this tumor was a myxoma and when removed did not return.

Von Volkmann. Cases credited by Powers to von Volkmann are the cases reported) by Fricke and Schuchardt.

34. Wrede, L. Orth Festschrift, 1903, p. 673.

Weinlechner. Powers gives Weinlechner credit for two cases, referring to them (1) Wiener klin. Wochenschrift, 1889, 109, 130; and Medical Press and Circular, 1888, i, 616. The first reference is to the paper by Kolisko, the cases being those he describes and publishes, the second is a mere mention of Weinlechner's having had a case and no doubt refers to the same two reported by Kolisko.

II. Infantile. *General or Miscellaneous.*

1. Amann, J. A. Archiv. f. Gynäkologie, 1907, lxxxii, 746.

2. Deck. Inaugural Dissertation, Zürich, 1908; also Münchener med. Wochenschrift, 1908, p. 137.

3. Heckford. Trans. Obstetrical Society of London, 1869, x, 224.

4. Holmes. Pediatrics, 1907, xix, 95; also Trans. Medical Association of Georgia, 1906, p. 304.

5. Marshall, L. W. British Medical Journal, 1889, ., 127.

6. Marullaz, M. Thesé, Lausanne, 1904.

7. Peyrache, J. Thesé, Paris, 1905.

8. Piechaud and Guyot. Revue mensuelle de Gynecologie, Obstetrique et Pediatric de Bordeaux, 1901, iii, 210; also Congres de Nantes, 1901; also Revue de Gynecologie et de Chirurgie Abdominale, 1901, iii, 210.

9. Strassmann. Berichte aus Gynäk. Gesellschaften u. Krankenhäusern, Gesellschaft für Geburtshülfe und Gynäkologie zu Berlin, April 28, 1899; Centralbl. f. Gynäkologie, 1899, xxiii, 654; Zeitschrift f. Geburtshülfe u. Gynäkologie, 1899, xli, 519, 986.

10. Waldstein, E. Archiv. f. Gynäkologie, 1899, lviii, 427; Centralbl. f. Gynäkologie, 1899, xxiii, 1552.

III. Adults.

1. Ahlfeld. Archives f. Heilkunde, 1867, viii, 560.

2. Alglave and Milian. Bull. Soc. Anat. de Paris, 1891, lxxiii, 651.

3. Amann, J. A. Kurzgefasstes Lehrbuch der Mikroskopische Gynäkologischen Diagnostik., Wiesbaden, 1897, p. 38.

4. Baiardi, D. Annali di Obstetricia, Ginecologia, e Pediatria, 1880, ii, 47.

5. Boldt, H. J. American Journal of Obstetrics, 1906, liv, 550; New York Obstetrical Society, May 8, 1906.

6. Favell. British Medical Journal, 1909, ii, 1677; also North of England Obstetrical and Gynecological Journal, Friday, November 19, 1909.

7. Ferrari. Sala Chir. d. osp. Magg. di Bergarno, 1891, p. 179.

8. Fraenkel. Deutsche Zeitschrift für prakt. Med., 1875, p. 77.

9. Francke, R. Inaugural Dissertation, Berlin, 1898, p. 93; Centralbl. f. Gynäkologie, 1899, xxiii, 825; Virchow's Archives, cliv, p. 363.

10. Gatti. Gior. della R. Acad. de Med. di Torino, 1892.
11. Gebhard. Path. Anat. der Sexualorgane, Leipzig, 1899, p. 555.
12. Gervis. In discussing the paper by Lewers (*q. v.*) mentions having seen a case in his own experience.
13. Gow. St. Bartholomew's Hospital Reports, 1891, xxvii, 97.
14. Herzfeld, C. A. Allg. Wiener med. Zeitung., 1889, xxxiv, 558.
15. Hofmokl. Wiener med. Presse, 1891, p. 1229.
16, 17. Horn, F. Monatsschrift f. Geburtshülfe u. Gynäkologie, 1896, iv, 409.
18. Jellett, H. Journal of Obstetrics and Gynecology of the British Empire, 1907, xii, 285.
19. Jellett and Earl. Trans. of the Royal Academy of Medicine in Ireland, 1904, vol. xxii.
20. Jones, Hanfield. In discussing the case reported by Lewers (*q. v.*), said that he had seen a case in St. Mary's Hospital.
21. Jones, H. Macnaughton. Lancet (London), 1902, i, 439.
22, 23. Jung. Centralbl. f. Gynäkologie, 1899, xxiii, 333; Monatschrift f. Geburtshülfe u. Gynäkologie, 1899, ix, Heft 3.
24. Kalustow. Archiv. f. Gynäkologie, 1891, xl, 499.
25, 26. Kaschewarowa-Rudnewa. Virchow's Archives, 1872, liv, 65.
27. Klein, R. Archiv. f. Gynäkologie, 1894, xlvi, 292.
Langdon. See case reported by Gow.
? Lewers, A. H. N. Trans. of the Obstetrical Society of London, 1886, xxviii, 78. (This tumor may have been secondary to a coexistent sarcoma of the uterus, and so has not been used in compiling the tables in this paper.)
28. Maclean, E. J. Jour. of Obstetrics and Gynecology of the British Empire, 1909, xv, 245.
29. Mann. American Journal of Obstetrics, 1875, viii, 541.
30. Meadows. Trans. of the Obstetrical Society of London, 1869, x, 141.
31. Mentzel. Centralbl. f. Gynäkologie, 1885, ix, 245.
32. Morris. Obstetrical Transactions, London, 1900, xlii, 144; mentions having seen a case in his discussion of Lea's paper.
33. Morris, C. A. Practitioner, 1908, ii, 393.
34. Müntz. Frauenarzt, 1894, ix, 297.
35. Morestin, H. Bulletins de la Société Anatomique de Paris, 1898, xii, 431.
36. Odebrecht. Berliner klin. Wochenschrift, September 1, 1890; Gesellschaft für Geburtshülfe und Gynäkologie zu Berlin, January 24, 1890.
37, 38. Oliver. Medical Press and Circular, 1892, liii, 475.
39. Parona. Annali Univ. med. Chir., Milano, 1887, 241.
40. Potherat. Bulletins et mémoir de la Société de Chirurgie de Paris, 1906, xxxii, 703.
41. Rashkes. Medycyna. Warszawa, 1903, vol. xxxi; J. Akush. i jensk. boliez, St. Petersburg, 1903, xvii, 1359 (abstract Centralbl. f. allg. Path. u. f. path. Anat., 1903, xiv, 657).
42. Rollin. Revue de Gynécologie, 1905, ix, 1055, 1087.
43. Rosenberger. Szüleszet és nögyogy, Budapest, 1908, p. 33.
44. Von Rosthorn, A. Wiener klin. Wochenschrift, 1889, ii, 729. This case is also referred to by Breisky, Krankheiten der Vagina, Deutsche Chirurg. Leif., 1886, p. 60
45. Rubeska, W. Centralbl. f. Gynäkologie, 1896, 113, N. 5.
46. Savage, Smallwood. British Medical Journal, 1899, ii, 1281.
47. Senn, N. American Journal of Obstetrics, 1895, xxxi, 565.
48. Seitz. Sammlung klinische Vorträge, Leipzig, 1900–3, No. 208, p. 76
49. Spodaro. Gaz. d. osp., Milano, 1887, viii, 275.
50. Simmons. Edinburgh Obstetrical Transactions, 1884 and 1885, x, 205.
51, 52. Spiegelberg. Archiv. f. Gynäkologie, 1872, iv, 348.
53. Steinthal, C. F. Virchow's Archives, 1888, cxi, 449.
54. Ter Neumann. Warfvinge Festschrift, Gothenburg, 1893, and 1895.
55. Underhill. Edinburgh Medical Journal, 1885, p. 485.
56. Wirt. Inaugural Dissertation, Bonn, 1891 (abstract Centralbl. f. Gynäkologie, 1892, xiv, 442.
57. Wirz. Inaugural Dissertation, Bonn, 1891.
58. Young, P. Edinburgh Medical Journal, 1885, p. 485.

PROGNOSIS OF TUBERCULOUS LESIONS INVOLVING THE WHOLE OF OR MORE THAN ONE LOBE.[1]

By Joseph Walsh, M.D.,

VISITING PHYSICIAN TO WHITE HAVEN SANATORIUM AND CONSULTING PHYSICIAN TO THE TUBERCULOSIS DEPARTMENT OF THE PHILADELPHIA GENERAL HOSPITAL, PHILADELPHIA.

Three years ago Dr. Stanton called my attention to the fact that cases of tuberculosis of the lungs with large lesions (lesions involving an amount of tissue greater than the right upper lobe) usually did better when these lesions were on the left than on the right. As soon as the idea was mentioned I realized that I could recall more patients who were doing well with large lesions on the left than on the right, but I withheld full agreement until I made a further study. Further study confirmed this idea, and in the discussion of "The Heart in Tuberculosis," and of "The Primary Location and Development of Tuberculosis in the Lungs," before the meeting of the National Association in Washington, May, 1909, both Dr. Stanton and I mentioned the fact. It was not until this year, however, that I made a complete study of my private cases with this point in view.

Out of 1500 private cases of tuberculosis of the lungs I found only 67 with large lesions which I had seen over a sufficiently long time to make positive statements in regard to the exact involvement and the result. A study of these cases shows the following:

Comparison of the Results in Cases with Large Lesions on the Left and Right Sides.

Involvement.	Result. Good.	Fair.	Bad.
Left upper lobe	1	2	3
Left lung	0	1	1
Left upper lobe and probably right apex	1	2	1
Left upper lobe and right apex	6	2	0
Left lower lobe and right apex	1	0	1
Left lung and right apex	2	2	0
Left upper and upper part of lower lobe and right upper lobe	2	0	0
Left lung and right upper lobe	1	0	2
Right upper and middle lobes	3	1	7
Right upper and upper part of lower lobe	0	0	2
Right upper and lower lobes	0	0	1
Right lung	0	0	4
Right upper lobe and possibly left apex	2	1	0
Right upper lobe and left apex	3	0	0
Right upper and upper part of middle lobe and possibly left apex	1	0	0
Right upper and middle lobes and possibly left apex	0	1	2
Right upper and upper half of left upper lobe	1	1	0
Right upper and middle lobes and upper half of left upper lobe	0	0	3
Right upper and upper part of lower lobes and upper half of left upper lobe	1	0	0
Right upper lobe and two-thirds of left upper lobe	0	2	0
Summary.... Large lesions on left	14(45%)	9(29%)	8(26%)
Large lesions on right	11(31%)	6(17%)	19(53%)

[1] Read before the Sixth Annual Meeting of the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May, 1910

This table shows that even when we compare lesions of the right upper lobe with those of the left the latter are more favorable, though the comparison is not exactly just, since the left upper lobe is considerably larger than the right. If we omit as we should have done lesions confined to the right upper lobe, that is, lesions not affecting the right middle or lower lobe, the cases with large lesions on the right would stand as follows:

	Result.		
Involvement.	Good.	Fair.	Bad.
Large lesions on right	5(19%)	2(8%)	19(73%)

In addition, further study of the individual cases shows that there was no coincidence of character or environment favoring the left-sided cases, but, on the contrary, the surrounding circumstances favored the right-sided cases. Even the fact that in the cases with bad result we included no case that died of an accident like hemorrhage, pyothorax or pneumothorax favored the right-sided cases.

In the classification of the results, good result means that the patient is well and has been pursuing his ordinary occupation for a period of from two years to five years, except in two cases which have been working only one year; fair result means that the patient has been well for one year, but is unable to work; bad result means that the patient has died or is hopelessly sick in bed.

Taking everything into consideration, therefore, I have no hesitation in thinking that large left-sided lesions more frequently give good results than large right-sided ones.

Dr. Stanton's personal statement at the National Association meeting last year was as follows: "I have long been convinced that a large left-sided lesion offered a better prognosis than a large right-sided lesion. The kind of a case I refer to is familiar to every one working in tuberculosis. One rather frequently sees patients with complete left-sided involvement with rales over both lobes and the apex beat palpable and visible as far out as the left anterior axillary line. The right chest in these cases is usually much larger than the left and has a much greater amount of motion. Such patients often have a practically normal pulse rate and are able to do nearly the normal amount of work. While such a case as this is not uncommon, I have never been able to find a patient with the same amount of involvement on the right side who was able to get even a moderate amount of strength."

Dr. Stanton's original explanation of a possible cause for the better prognosis was: With large left-sided lesions the heart is drawn to the left, but this displacement is merely a drawing to the left and disturbs in no way the normal relation of the heart and vessels to each other; when, however, the heart is drawn to the right by a large right-sided lesion the relation of the heart to the vessels is disturbed by the heart turning on itself instead of merely

allowing itself to be drawn in a normal position. This turning over of the heart so that the apex, instead of pointing to the left, points to the right twists the vessels, with the consequence that extra work is put on the heart. This extra work on the already overworked heart is what changes the prognosis from favorable to unfavorable. This explanation appealed to both of us because we realized how much the heart has to do with making the prognosis favorable or unfavorable.

During the last year, however, in a careful study of the hearts of seventy-five autopsied cases dying of tuberculosis of the lungs, we found that the heart never did turn on itself, and when displaced to the right it appeared to be displaced, so far as we could see, in practically the same fashion as when it was displaced to the left. This explanation, therefore, fell to the ground.

A second explanation which I thought might mean something, and which I stated last year at the meeting of this Association, is that large right-sided lesions usually represent an acute or a subacute progression of the disease with little or no resistance, and large left-sided lesions are usually in cases which have advanced on account of causes not connected with the disease, like environment, etc., and which show that their susceptibility to tuberculosis is not great by the fact that they have already cured or practically cured a lesion at the right apex. The frequency of these cases is due to the frequency of the primary lesion at the right apex.

In the study last year of the primary location and development of tuberculosis I tried to show that clinical tuberculosis of the lungs has its primary seat more frequently at the top of the right than at the top of the left lung; that this lesion usually heals or almost heals, and in healing throws about itself a special resistance, so that if for any reason further dissemination occurs, it is usually implanted at the apex of the opposite lung. In exceptional cases the individual is too susceptible or the lesion too virulent to admit of healing, and the process extends acutely throughout the whole or a large part of the upper lobe, or even of the lung on the first side. In other exceptional cases, after half healing at the apex the resistance of the individual disappears, the half-healed lesion breaks down, and continues to advance on the same side. In the first or usual way of development the prognosis is better than in either of the latter ways.

Moreover, this explains some of the discrepancies we have found, for although, as a rule, large left-sided lesions give a good prognosis, there are exceptions to this rule, as is very evident in a study of the table, which are not to be explained by the mere extent of the lesion.

In addition, further study of the table shows that the cases which gave the best results were those in which there was a large lesion on the left with chronic involvement of the right apex, or a large lesion on the right with chronic involvement of the left apex; while

the cases that gave the majority of bad results were cases with large lesions on the left without any lesion on the right, or cases with large lesions on the right without any lesion on the left.

Rearranging the table on page 589, we find a large lesion in one lung with none in the other in 26 cases, a large lesion in one lung and a doubtful lesion in the other in 11, and a large lesion in one lung and a small or medium sized lesion in the other in 30. Omitting the middle category, since the lesions are not positive, we have:

COMPARISON OF THE RESULTS IN CASES WITH A LARGE LESION IN ONE LUNG ONLY, AND A LARGE LESION IN ONE LUNG WITH A SMALL OR MEDIUM SIZED LESION IN THE OTHER.

	Result.		
Involvement.	Good.	Fair.	Bad.
Large lesion in one lung only	4(15%)	4(15%)	18(69%)
Large lesion in one lung, small or medium-sized lesion in other lung	17(57%)	7(23%)	6(20%)

There have been several pathological papers written to show that the primary lesion of tuberculosis in the lungs is as frequently at the top of the left lung as at the top of the right, among which one of the most recent and most conclusive is that of Adami and McCrae before the International Congress on Tuberculosis in Washington in 1908.

Out of 1000 cases autopsied, 417 showed evidence of past or present tuberculosis in some organ. Of these 417, 100 cases showed small areas of calcification or fibrosis in the lungs; in other words, small healed lesions; 72 cases showed small areas of caseation, but without recent activity; in other words, latent disease. In these 172 cured, or practically cured cases the lesions were slightly more frequently on the left than on the right. The writers do not state the frequency with which the different sides were involved by the more advanced lesions; in other words, their statistics are strictly limited to pathological lesions.

In this paper, however, I am considering clinical lesions. I would be unwilling to consider a case with a cured tuberculous wart on his finger as a cured case of clinical tuberculosis, and in like manner, am unwilling to consider a spontaneously cured single tubercle in the lung as a cured case of clinical tuberculosis. As the situation of the tuberculous wart depends not on the greater susceptibility of the right or left hand, but on the accident of inoculation, so I believe such tubercles as they describe in the lungs may be due to the same cause. Despite the pathological findings, therefore, I believe that clinical tuberculosis, that is, tuberculosis in cases with some susceptibility, begins more commonly at the top of the right lung.

In addition, a study of the progression of tuberculosis of the lungs on autopsies at the Phipps Institute showed that in the cases in which it was possible to judge the progression, the progression commonly corresponded to what I have pointed out as the most fatal clinically; in other words, the majority of the cases showed progression practically throughout one side before the other was involved. I do not wish to emphasize this fact, however, since this study of the progression from a pathological standpoint was not very satisfactory on account of the number of cases in which the progression could not be judged.

In the discussion of this subject last year the idea was suggested that the cases of large involvement which did so well might have been cases with thickened pleura instead of actual lung involvement. In answer to this I would say that practically all the cases presented in this paper, especially those with very large lesions, were examined not only by me, but by others (Dr. Flick, Dr. Stanton, etc.), and after the last seven years' experience with autopsies in which we have seen our clinical diagnosis practically constantly confirmed I am not willing to grant even the possibility of this.

In addition, I might add that I have studied the cases from the standpoint of cavity formation and other special features in connection with both the disease itself and the circumstances of the patient, like age, sex, environment, etc., and have found nothing further to account for the better result in the left-sided cases.

Conclusions. 1. Lesions involving the whole of one lobe of the left lung usually give better results than lesions of the same size in the right lung. One reason for this appears to be that the large lesion on the left more frequently represents the secondary development in a somewhat resistant case.

2. Lesions involving an amount of lung tissue the size of the left upper lobe give a better prognosis when the opposite side shows a chronic healed lesion.

REVIEWS.

THE EXPECTATION OF LIFE OF THE CONSUMPTIVE AFTER SANATORIUM TREATMENT. By N. D. BARDSWELL, M.D., M.R.C.P., F.R.S., Medical Superintendent of the King Edward VII Sanatorium. Pp. 130. Edinburgh, Glasgow, and London: Henry Frowde and Hodder & Stoughton, 1910.

THE book comprises statistical details and the life histories in brief of 241 patients. From the beginning of the author's sanatorium work he attempted, year by year, to keep in touch with the physical condition of the discharged patients, and in this he has met with a fair degree of success. As to the stage of disease, the classification employed is that adopted by the National Association, while the manner of tabulating after-results is along the lines adopted by the Germans. Some of the tables show the physical condition of the patients, the effects of different occupations, and their capacity for work at the end of four to seven years after discharge. The life histories are classified according to incipient, moderately advanced and far advanced stages. From one who has had considerable experience in the sanatorium treatment of tuberculosis, the book is of interest particularly in noting the "post-sanatorium life" of the patients and its effects. The author epitomizes the results of his efforts, which are obviously painstaking, with the statement that he is unable on account of insufficient evidence to estimate the average length of "post-sanatorium life." The book presents the subject, which has received but little attention in England and America, in a systematic and attractive manner.

W. T. C.

AN ANATOMICAL AND SURGICAL STUDY OF FRACTURES OF THE LOWER END OF THE HUMERUS. By ASTLEY P. C. ASHHURST, M.D., Prosector of Applied Anatomy in the University of Pennsylvania, Philadelphia. Pp. 158; 150 illustrations. Philadelphia: Lea & Febiger, 1910.

IN this, the Samuel D. Gross Prize Essay of the Philadelphia Academy of Surgery for 1910, the author has made a careful analysis of fifty-six cases of fracture of the lower end of the humerus which have come under his care in the various dispensary services in which he has been working. They are illustrated by a large number

of good skiagrams, plates, and diagrams. No claim is made for originality, either in diagnosis or treatment, beyond the careful and systematic examination of his cases, which is so characteristic of Dr. Ashhurst's work. His classification of these injuries is based on good anatomical and morphological lines. In the directions which are so clearly outlined for the treatment of these injuries, namely, the position of hyperflexion which was routinely employed because it is the one position in which the fragments are retained accurately in place without the aid of pads, splints, etc., the results obtained will be in marked contrast to the usual methods now pursued; so that the average practitioner may approach the treatment of injuries of this character with the expectation of obtaining a good functional result in a large percentage of the cases treated. The work evidences the greatest care and accuracy, and is invaluable to the practising surgeon and teacher. It is also an inspiration to young men just entering upon their careers, who have perhaps only a dispensary service, for it shows them what valuable material is to be found in every clinic, requiring only the careful noting, study, and classification so exemplified in these fifty-six cases of injury of the lower end of the humerus collected by the author. The general arrangement of the cuts and plates reflect great credit on the publishers, and we commend the work most heartily to all persons interested in this class of injuries. R. H. H.

PULMONARY TUBERCULOSIS AND SANATORIUM TREATMENT. By C. MUTHU, M.D., M.R.C.S., L.R.C.P., Physician to Mendip Hills Sanatorium, etc. Pp. 201; 10 illustrations. London: Baillière, Tindall & Cox, 1910. New York: William Wood & Co., 1910.

THE author has prepared the volume in three parts, which deal with the scientific, the sanatorial and the social aspects of tuberculosis. Verses of several well known poets have been used in a pertinent manner to introduce many of the chapters. Though the subject comprising the so-called scientific section is taken up in a systematic, clear, and comprehensive style, there is much for adverse criticism. The author unduly emphasizes the importance of heredity. He states that the symptoms of tuberculosis may spontaneously arise from the evolution of the common forms of bacilli (also pneumococci) in the tissue without direct infection with the tubercle bacillus—an extraordinary statement. This he designates as "spontaneous tuberculosis." The term "contagious" is not employed with its usual significance. In Part II every aspect of sanatorium treatment is considered, including inhalation and electrical treatment. However, one questions the potency of formaldehyde in curing tuberculosis through hardening of the mucous

membranes. But little reference is made to drug therapy, aside from inhalants, while considerable emphasis is made in a lengthy section upon walking and respiratory exercises, both of which are objectionable from the quantitative standpoint. The nucleus of Part III is made up of suggestions relative to social reforms, and these are stated so clearly, forcefully, and intelligently that one enthuses in approbation of his plans. As a whole, the book shows in a well systematized, although in some instances not scientifically commendable, text the subject of tuberculosis and the author's detailed experience in sanatorium treatment. W. T. C.

THE PRINCIPLES OF GYNECOLOGY. By W. BLAIR BELL, B.S., M.D., Assistant Gynecological Surgeon to the Royal Infirmary, Liverpool. Pp. 551; 363 illustrations. London: Longmans, Green & Co., 1910.

"OF the making of books there is no end," and it is a great pity. By far the larger number could be well spared. Only rarely does a book appear above the horizon of the reviewer which can justify its existence. This being the case, it will readily be realized how pleasurable has been the work of the reviewer in this instance, as this book may be justly said to be one of the best for the use of students and general practitioners as yet published. The first three chapters are devoted to the evolution and development of the female generative organs, together with their anatomy and physiology. Chapter IV is concerned with history-taking and methods of examination, while Chapters V to VIII inclusive deal with the congenital and acquired derangements of the normal anatomical and physiological conditions of the pelvic organs. In the last mentioned chapter, when discussing certain disorders of menstruation, the author allows his enthusiasm to run away with his judgment to some degree in the advocacy of the calcium therapy; while there is no doubt that the work done in recent years upon the physiology of the ductless glands is pregnant with possibilities, there is still too much that is uncertain and too much completely hidden to allow of quite as much definiteness of opinion as is expressed by the author. The whole subject, however, is intensely interesting and the enthusiasm is easily forgiven.

The chapters immediately succeeding are concerned with the disorders of the normal physiological conditions as related to conception, with the infective and parasitic diseases of the genital tract and with neoplasms, both innocent and malignant, together with the allied morbid conditions. Chapter XV deals with the preparation of a patient for operation and her subsequent care. The only criticism of an adverse nature is that it would be well

to drop calomel from the postoperative routine. Chapter XVI, comprising 71 pages, is a synoptical description of the main principles of gynecological operative procedures, together with some details of their technique. In the main there is nothing but commendation for this portion of the work, though it seems a pity that ventrosuspension is not alluded to and that a few interrupted silkworm-gut sutures are not advocated in the layer method of abdominal closure.

The book closes with an appendix of five pages upon electrotherapeutics as applied to gynecology, and one of ten pages in which the causes of certain cardinal symptoms are classified, as, for instance, hemorrhage, amenorrhœa, etc. Throughout the whole volume the author has in an almost unexampled manner linked the cognate subjects of gynecology and obstetrics, thus enhancing the value of the work many times. We can only end as we began, by saying that the book is one of the best that we have ever read upon this subject. W. R. N.

NEPHROCOLOPTOSIS. A DESCRIPTION OF THE NEPHROCOLIC LIGAMENT AND ITS ACTION IN THE CAUSATION OF NEPHROPTOSIS, WITH THE TECHNIQUE OF THE OPERATION OF NEPHROCOLOPEXY, IN WHICH THE NEPHROCOLIC LIGAMENT IS UTILIZED TO IMMOBILIZE BOTH KIDNEY AND BOWEL. By H. W. LONGYEAR, M.D., Professor of Gynecology and Abdominal Surgery in the Detroit Post-graduate Medical School. St. Louis: C. V. Mosby Company, 1910.

THE author looks upon the nephrocolic ligament as the principal etiological factor in the production of nephroptosis; further, because of the action of this ligament, he believes that nephroptosis must invariably be the result of coloptosis, except when due to trauma, and, consequently, he has coined the term nephrocoloptosis to indicate the co-relation existing between these two conditions. He describes the nephrocolic ligament and gives directions for its demonstration upon the cadaver. The anatomy and pathology of the kidneys and adjacent viscera are considered in so far as they bear upon the subject under discussion. The primary etiological factor in the production of nephroptosis is relaxation or absence of the hepatocolic ligament, which permits the cecum and ascending colon to sag and to exert traction on the kidney through the nephrocolic ligament. Nephrocoloptosis manifests itself chiefly through gastric and colonic symptoms, which the author details clearly and accurately. With the exception of Dietl's crises, the kidney participates but little in the clinical picture. The skiagraph is invaluable in the diagnosis of coloptosis. In his preface the author

asserts that very few general practitioners know how to examine for nephroptosis, and the reader anticipates with interest the description of a new method; the procedures described are generally known and employed. Treatment may be prophylactic, medical, and surgical. The author's method of suspending the colon and kidney by means of the nephrocolic ligament is described and excellent illustrations demonstrate the various steps of the operation. It is difficult to comprehend how this operation can produce such remarkable results as are reported in fifty-six cases. Were the chief manifestations referable to the kidneys, one might understand how suspension by this method could give relief. When one considers, however, that the symptoms detailed are largely due to ptosis and angulation of the colon, malformations which the operation does not correct, one is forced to the conclusion that the author has read his results through the eyes of an enthusiast. F. E. K.

KLINISCHE UND ANATOMISCHE BEITRÄGE ZUR LEHRE VOM UTERUSMYOM. Von DR. MED. ANTON GARKISH. Berlin: S. Karger, 1910.

THIS monograph of 148 pages comprises an analytical study of 399 cases treated in the German Gynecological Clinic at Prague from 1900 to 1908. The first portion is devoted to the various clinical manifestations of myomata, which the author discusses in a thorough and interesting manner. Statistics are at times burdensome but impossible of elimination in a work of this nature. After defining the indications and contraindications for the various operative procedures, he tabulates the postoperative morbidity and concludes that spinal anesthesia and short confinement in bed are potent factors in reducing the number of pulmonary complications and thromboses during convalescence. The subsequent examination of 225 patients demonstrates the value of conserving one or both ovaries, especially in women under forty years of age. With the exception of a brief presentation of prevailing views concerning the histological aspects of myomata, including their degenerations and associated alterations in the endometrium, tubes, and ovaries, the second portion is devoted to the enumeration of a long series of detailed case histories, operations, and histological findings—a fault so frequently encountered in such monographs. While this contribution adds nothing new to our knowledge of myomata, it represents painstaking efforts in accurately summarizing the data presented by a large gynecological clinic, and is of value in that it confirms existing ideas regarding one of the most important pathological changes found in the uterus. F. E. K.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

REGIUS PROFESSOR OF MEDICINE, OXFORD UNIVERSITY, ENGLAND,

AND

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND.

An Early Sign of Aortic Sclerosis.—N. G. KUKOVIEROFF (*Russki Vrach*, No. 51, 1910) reports a new sign of beginning arteriosclerosis of the aorta which has not hitherto been noted. Out of more than 2000 cases he was able to diagnosticate early sclerosis in 164 patients not presenting the ordinary physical signs of the lesion. The diagnosis was corroborated by the later history of the cases and by radioscopy. The signs consisted of a systolic bruit heard over the course of the beginning aorta and over the sternum about the second and third costal cartilages when the arms are *raised* above the head. The bruit comes from the root of the aorta and is due to changes in vibrations of the blood column produced by the sclerotic changes and accentuated by the position of the arms. This sign has the same significance as the ordinary systolic murmur heard in patients with sclerosis of the aorta, but it is of *importance* because it is present—as in the 164 cases reported—in patients who do not give other evidence of the lesion, and is an *early* sign. It is, however, carefully to be differentiated from the venous hum or cardio-respiratory murmurs sometimes heard in this region.

Autoserotherapy in Serofibrinous Pleurisy.—N. T. CHIGAYIEFF (*Russki Vrach*, 1910. No. 51) reports 56 cases in which this treatment was essayed. Of these, 6 were failures. In 8 the results were unsatisfactory. In 42 the absorption of the effusion was complete and rapid. In 15 of the 42, only one injection was required; in the rest from two to four injections. The author comes to the conclusion that subcutaneous auto-inoculation with the patient's exudate, whether in tuberculous or non-tuberculous cases, is quite harmless and causes neither local nor constitutional disturbances of any importance. There may follow a slight rise in temperature, but this amounts to no more

than a fraction of a degree. In patients with pulmonary tuberculosis, no changes in the tuberculous process are noted, In the majority of cases absorption of the effusion begins very soon after the subcutaneous injection. The pleurisy is healed in from two to three weeks, sometimes in one week—although it had been of long standing. The earlier the injections are made the sooner is the pleurisy cured. The absorption of the effusion is marked by increased diuresis; subjective symptoms are in all cases improved.

A New Test for Cancer of the Stomach and the Tryptophan Test. — OPPENHEIMER (*Deutsch. Archiv. f. klin. Med.*, 1910, ci, 293) relates his experience with the glycyltryptophan test of Neubauer and Fischer for the detection of cancer of the stomach. His results were, on the whole, very satisfactory. One interesting case with gummata of the left lobe of the liver but no cancer (operation) is recorded, in which both tryptophan and acetic acid test (vide infra) were positive. Oppenheimer has discovered a new test which gives practically the same results as the tryptophan test. The procedure is the following: Forty minutes after an Ewald breakfast, the stomach is emptied and the contents filtered. To the clear filtrate one adds 3 per cent. acetic acid cautiously, a drop at a time. In case the reaction is positive, a turbidity or cloud appears which vanishes only after considerable acetic acid or a little hydrochloric acid is added. Dilution with one to five volumes of distilled water causes the cloud to remain. The only source of error is mucus which also gives a cloud with acetic acid; but this cloud is unaffected by the addition of a few drops of HCl and does nor occur in high dilution of the gastric contents. If the gastric filtrate is so turbid that dilution with an equal quantity of distilled water does not clear it the acetic acid test cannot be employed. Slow filtration through a wet, folded filter usually yields a clear filtrate. Oppenheimer has not determined the cause of the reaction. In all cases where the tryptophan test was positive, the acetic acid test was also given (except where turbidity of the filtrate precluded its employment), including the case of hepatic gummata. The test may be applied to vomitus, and blood and pancreatic juice are not disturbing factors as in the glycyltryptophan test.

Lipemia in Diabetes. — KLEMPERER (*Deut. med. Woch.*, 1910, xxxvi, 2373) has investigated the lipemia which so frequently accompanies acidosis in diabetes. From observations on a fairly extensive material he has shown that lipemia causes large quantities of cholesterin and lecithin to appear in the blood plasma. These substances are not derived from the subcutaneous fat. There is no diminished fat destruction (consumption) on the part of the organism. The increase in blood lipoids Klemperer attributes to the heightened cell metabolism in severe diabetes. Cell katabolism throws the lipoids into the blood stream from which they are removed by the anabolic activity of the body cells. Thus the lipemia results from the mobilization of lipoids in the body.

Intrathoracic Struma. — KREUZFUCHS (*Münch. med. Woch.*, 1911, lviii, 23) finds intrathoracic struma not infrequently in Vienna. Of 1040 Röntgenologic examinations (both thoracic and abdominal) in

the last seventeen months, 1.25 per cent. were pure substernal strumas. In five other cases a process from a cervical goitre extended beneath the sternum. The symptoms of intrathoracic struma are largely the result of pressure. Dyspnea was the most constant complaint and was often independent of exertion. "Dyspnea in the absence of disease of the lungs or circulatory system should always suggest substernal struma." Palpitation of the heart is frequent but is nearly always associated with the shortness of breath. Dysphagia is commoner than might be supposed. It is seldom so severe as in cancer of the thyroid, and regurgitation is rare. Hoarseness from paralysis of the recurrent laryngeal, stridor from tracheal stenosis, and cough are less frequent, though important, symptoms of substernal struma. Likewise dulness under the sternum, dilatation of the veins in the neck and on the upper anterior chest wall, redness and puffiness of the face, and cyanosis of the lips are found in a small proportion of the cases. Inequality of the radial pulses is a rare symptom. In the literature a few other symptoms are reported, such as unilateral exophthalmos with unilateral sluggishness of the pupil, prominence of a clavicle or the sternum, and fixation of the larynx. Though perhaps not common, a low position of the larynx is very important and appears to be pathognomonic. It must be remembered that with cervical struma it happens at times that the gland extends beneath the manubrium sterni to a sufficient extent to cause all the symptoms enumerated above.

Intravenous and Subcutaneous Administration of Dextrose.—KAUSCH (*Deut. med. Woch.*, 1911, xxxvii, 8) has had gratifying results from subcutaneous or intravenous administration of glucose in patients unable to retain food in the stomach or rectum. No complications or sequelæ have occurred in more than 40 cases. The sugar is dissolved in 0.85 per cent. sodium chloride solution, filtered, and boiled to sterilize it. For subcutaneous use, Kausch employs 1000 cc. of a 2 per cent. sugar solution. The percentage can be increased gradually to 5. Intravenous injections of 1000 c.c. of 5 to 7 per cent. glucose are well borne. If an 8 or 10 per cent. glucose solution is used, 2 to 10 per cent. of the sugar injected is excreted in the urine. In some cases the author has used two intravenous injections of one liter daily. The subcutaneous infusion is no more painful than plain physiological salt solution. While the author's experience has been confined to surgical cases, he recommends that this method of feeding be extended.

Generalized Syphilitic Infection of Rabbits.—UHLENHUTH and MULZER (*Deut. med. Woch.*, 1911, xxxvii, 51) have made important studies upon experimental lues in rabbits, the result of which they summarize as follows: They have succeeded repeatedly in producing a generalized syphilitic infection in rabbits. Young animals, especially when infected by the intracardiac method described by the writers, have yielded the most constant results. The experimental disease is characteristic. Nasal and caudal tumors are observed which are similar to human gummata histologically. The emaciation, paronychia, and papulo-ulcerative syphilides all remind one of hereditary lues in man. In all of these lesions the spirochetæ are demonstrable. Furthermore, the authors have succeeded in obtaining living Spirochetæ pallidæ

from the circulating blood in experimental syphilis. The results should be valuable in the study of chemotherapy, in the study of hereditary lues, of parasyphilitic nervous affections, immunity, etc. By repeated passage of the spirochetæ through successive animals, it has been possible to increase the virulence of the organisms.

The Bearing of Old and New Facts Upon Our Conceptions of Cardiovascular Disease —In the past the heart received first attention and the vessels were considered last in importance. HARE (*Interstate Med. Jour.*, 1911, xviii, 277) now believes that the pendulum has begun to swing in the opposite direction and the careful study of the vessels will give as much information as is obtained by direct examination of the heart. Following along the line pursued in a recent report in the *Therapeutic Gazette* (June, 1910) on the value of studying the blood pressure in pneumonia for the purpose of determining the state of the heart muscle and the need for stimulation or cardiac support, he emphasizes the great importance of the use of the sphygmomanometer. A daily record of the patient's circulatory state is possible, and any tendency to circulatory failure can be discovered early and promptly combated. He calls attention to an important observation made by Gibson: "A pressure appreciably below normal in pneumonia is invariably of evil omen, and any considerable fall bodes disaster. When the arterial pressure, expressed in millimeters of mercury, does not fall below the pulse rate expressed in beats per minute, the fact may be taken as an excellent augury; while the converse is equally true." In all cases of pneumonia in which the blood pressure fell to the pulse rate, or below it, active stimulation is instituted. When the blood pressure bore a normal ratio to the pulse rate, and the heart sounds were satisfactory, no drugs were resorted to. Regarding the use of drugs, much caution should be exercised in the giving of nitrites and they should only be used in cases where the pressure is so high that there is fear that the heart will become exhausted in trying to drive the blood through the narrow blood paths. He emphasizes two important facts in the use of digitalis. This drug powerfully stimulates the vagi and so primarily slows the auricles and indirectly the ventricles. The auricular walls themselves are very little stimulated if at all, but the ventricular walls are powerfully stimulated and are caused to beat more forcibly and if the ventricular walls are cut off from the vagus influence by injury to the bundle of His, they also contract more frequently under digitalis than before the drug is given. The use of digitalis in a case of partial heart block may precipitate a fatal attack of the Stokes-Adams syndrome, while in cases in which there is complete destruction of His' bundle, or complete heart block, digitalis may be advantageous, since the ventricles are no longer in the slightest degree under control of the auricles and are increased in power and in frequency of contraction and are able to supply the body with greater volume of blood. This fact is well borne out by the experimental work of von Tabora. In conditions in which the cardiac conductivity is decreased, there seems to be little doubt that digitalis still further impairs it. In the case of a patient suffering from circulatory failure due to mitral stenosis, after carefully weighing the import of the heart sounds, instruments of precision should be used to determine if possible whether there

is any delay in the transmission of the contraction impulse over His' bundle. If such a delay exists, great care should be exercised in the use of digitalis, and if the drug is given at all, the dose must be so small as to produce a very gradual effect, one which will not consist in decreasing auricular contraction through vagal stimulation, but gently reëstablish general cardiac power.

On Chylous and Pseudochylous Ascites. — Through an extensive search of the literature, WALLIS and SCHOLLBERG (*Quarterly Jour. of Med.*, 1910, Part I, iii, 301; 1911, part II, iv, 153) have traced 171 cases of chylous and pseudochylous ascites. This number includes 3 cases coming under their own personal observation and in which they made exhaustive chemical examination of the fluid obtained through tapping. In addition they have given synopses of 60 cases of chylous and pseudochylous hydrothorax, and 8 cases of milky pericardial effusion recorded in the literature. Their conclusions are as follows: Milky ascitic fluid may be recognized in two main types—chylous and pseudochylous. The milky appearance of the latter is not due to free lecithin, fat, or a mucinoid substance, but to a lecithin globulin complex, which is held in suspension by the inorganic salts present in the fluid. By dialysis these inorganic salts may be removed, the lecithin globulin complex precipitated and the opalescence of the ascitic fluid disappears. The marked resistance of the fluid to putrefaction is due to the presence of lecithin. The prognosis in cases of milky ascites is grave and the mortality reaches 70.4 per cent. in cases of pseudochylous ascites, and 66 per cent. in chylous ascites. No specific morbid anatomy lesion may be said to be characteristic of milky ascites. In order to differentiate with certainty between the two types of milky ascites, a complete chemical and physical examination is necessary, and the results obtained seem to have a direct bearing on the question of the chemical physiology of the blood serum, particularly with regard to the serum proteins and carbohydrates present. In comparing the two main groups of milky ascites we find the following most distinctive features: Chylous ascites tend to accumulate more rapidly and the emulsification present is less perfect. The degree of opalescence is more or less constant and does not show the variations of the pseudochylous fluid. The odor of the fluid corresponds to the odor of the food ingested, while the pseudochylous ascitic fluid is odorless. Few cellular elements are found in the chylous fluid, and both types contain fine fat globules. On standing, chylous fluid exhibits a distinct creamy layer. This may or may not be present in the pseudochylous fluid, and in the latter the opalescence is not affected, and frequently a sediment settles out. The specific gravity of chylous fluid is usually higher than the pseudochylous type, and generally exceeds 1.012. The depression of the freezing point approximates that of chyle, while that of the pseudochylous more nearly corresponds to the figures of blood serum. The total solids vary considerably but are usually greater than 4 per cent. for chylous fluids and rarely exceed 2 per cent. for pseudochylous. Globulin occurs only in traces in chylous ascites and the total protein content generally exceeds 3 per cent. The protein constituents in pseudochylous fluids vary between 1 and 3 gram per cent. Mucinoid substances are absent in chylous fluids, but sometimes are found present in the pseudochylous

groups. The fat content in chylous fluid is generally high, and the fat corresponds to the fat contained in the food. In the pseudochylous fluid the fat content is low and may be present in traces; its melting point and chemical composition proves it to be pathological fat. Cholesterin is the invariable characteristic lipine to be found in the chylous fluid and lecithin occurs in traces. Lecithin exists in larger quantities in the pseudochylous type. No evidence of the lipine globulin combination is to be found in chylous ascites. Such a combination is present in the pseudochylous fluid, and is the cause for the opalescence and the resistance to putrefaction. The salts and the organic substances approximate the value found for chyle from the thoracic duct. While in the case of pseudochylous fluid they correspond more closely to the lymph and serous fluid.

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The Origin and Treatment of Ischemic Contracture and Gangrene.—BARDENHEUER (*Deut. Ztschr. f. Chir.*, 1910, cviii, 44) says that the contracture is due to the ischemia, but more especially to the venous stasis dependent upon it and to the influence of the carbonic acid on the nuclei of the muscle fibers. The ischemic infiltration is induced by the obstruction of the venous blood rich in carbonic acid. The stasis and ischemic infiltration result from the wounding of the arteries, chiefly by an intima rupture of the main vessels. However slight it may be, as from the application of a tourniquet, this suffices to produce ischemic contracture. The importance of the intima rupture depends upon the size of the wounded vessel. The more central the intima rupture, the greater is the stasis and the danger of gangrene, as well as the disturbance of nerve conduction from the venous stasis along the nerves. Ischemic contracture occurs also after partial or total tearing of the whole thickness of the arterial wall, although this cause is a very rare one, at least of isolated ischemic contractures. It is generally followed by total gangrene or the formation of a traumatic aneurysm. Ischemic myositis may develop after a simple contusion of the arterial and venous walls with small simultaneous injury to the collateral vessels, the bed of the vessels, and a secondary infiltration, traumatic and inflammatory in character. The arterial circulation need not be interrupted. Usually one speaks of ischemia of the flexors, but when the stasis is severe the extensors may also be involved. The pathogenesis of ischemic infiltration (myositis) is as follows: In consequence

of a central interference of the blood current, usually as a result of a severe wounding of the vessel bed, as from a supracondylar fracture, there develops a peripheral stasis of the limb, first in the venous trunks below the elbow. The stasis extends from here to the adjacent muscles, the flexors, and in the vessels even to the capillaries and arteries, so that the arterial current becomes more and more slowed. The ischemic myositis always lies below the central cause and below the joint, lying next below. The blood obstructed in the capillaries destroys the nuclei in the capillary walls, so that they become permeable to the blood serum which exudes, and the stasis and tension in the muscles are further increased. The diagnosis of an ischemic myositis depends upon the recognition of a central cause of the disturbance of the blood current, recognition of the acute ischemic myositis, the ischemic contracture, and the accompanying nerve affections. The recognition of the central cause is very important for the preventive treatment, as no constricting bandage should be employed in the presence of such a condition. Upon the first development of the acute myositis, the infiltration and tension at the site of the central cause must be relieved. It may be necessary to make incisions in the fascia and muscles for this purpose. After fibrous degeneration of the muscles appears, one of several operations may be performed to lengthen the contracted muscles or shorten the bones.

Calculous Anuria in a Case of Single Kidney, Treated and Cured by Ureteral Catheterism.—ANDRE (*Ann. d. mal. d. org. gén.-urin.*, 1911, i, 132) says that the classic treatment of calculus anuria is nephrectomy, practised as soon after the beginning of the symptoms as possible. Those who are in the habit of employing the ureteral catheter have the opportunity of trying this method before resorting to the knife. Cures by it have been reported. If it is not successful, operation can then be carried out without exposing the patient to the danger of much delay, as the passing of the catheter takes only a short time. A man, aged forty-two years, entered the hospital, September 22, 1910, because he had not been able to pass urine for forty-eight hours. Six years before he had suffered from renal colic for the first time, and two months later had another attack, in which he passed a calculus about the size of a pea. For three days preceding the beginning of the anuria in this attack he had passed discolored and turbid urine, when he was taken with severe pains in the hypogastric and iliac regions, especially on the left side. On September 20 he urinated only once. From then until his entrance into the hospital he did not pass any urine and his pain was persistent. A catheter introduced into the bladder did not evacuate any urine. The left ureter was catheterized immediately, the catheter penetrating easily into the renal pelvis without encountering any obstacle, and from it escaped urine with some force, indicating that it had been retained in the pelvis under some tension. This continued until 70 grams had escaped, then drop by drop. The ureteral sound was left in place and the patient carried back to bed. In the first twenty-four hours the total quantity passed by the sound was 1800 grams. During the following twenty-four hours it was 2600 grams. On the other hand, the patient passed spontaneously 1850 grams on the first day and 500

grams on the second day. After forty-eight hours the catheter was removed and the patient urinated easily and abundantly. The kidney which had been blocked manifested a hyperactive secretion. On September 29 a careful and prolonged cystoscopic examination failed to find the orifice of the right ureter, and it was concluded that there was probably no right kidney. Shortly afterward the patient was discharged well. He did not pass a calculus, and a skiagraph taken of the left kidney was negative. There was probably a small calculus present. It is the small calculi which usually provoke anuria.

A New Gastrostomy Operation.—LAFARO (*Deut. Ztschr. f. Chir.*, 1911, cviii, 307) makes an incision in the abdominal wall in the median line, from the tip of the xyphoid cartilage downward three or four inches. The left hand is then introduced into the wound and the abdominal wall on the left side grasped between the middle finger and thumb. In this way the left rectus muscle is located. With a long tenotome an opening is made through the substance of the left rectus from the wound surface to emerge on the skin surface a few centimeters within the outer border of the rectus. This opening is widened by cutting upward and downward and dividing the rectus into two equal layers, an anterior and a posterior. The size of this passageway should correspond to that of the portion of the stomach which is to be drawn through. This portion of the stomach is then drawn through with a suitable forceps and its base sewed to the posterior edge of the median end of the passageway with three catgut sutures. The opposite surface of this base is then sutured to the peritoneum and rectus on the opposite side of the median wound. The deep edges of the upper and lower portions of the median wound are then brought together by sutures. The end of the projecting portion of the stomach is now conducted through the tunnel made for it in the rectus muscle and skin and its apex is fastened to the skin edges of the small lateral external opening. The large median wound is then closed over the projecting portion of stomach by two layers of sutures, one for the fascia and the other for the skin. Finally, the emerging end of the stomach is opened and its edges sutured to the skin. This operation provides a strong, permanent sphincter for the gastrostomy opening and makes it continent.

Ligation of the Vein in Portal Thrombosis from Appendicitis.—SPRENGEL (*Zentralbl. f. Chir.*, 1911, xxxviii, 33) reports a case similar to that in which Wilms ligated the veins passing from the ileocecal region to the liver for the relief of symptoms of liver sepsis following the evacuation of a periappendicular abscess. Sprengel had operated for a perforative appendicitis. The symptoms of a portal vein phlebitis were apparent nine days later, and four days after this, or thirteen days after the first operation, he did a second operation. The drainage wound was thoroughly irrigated, cleansed, and closed by suture. A transverse incision was then made to the left, beginning about the middle of the original wound and passing through the right rectus and into the left rectus. The intestines were carefully packed off. Pressure on the cecum opened up the old focus of inflammation. A mesentery for the cecum and ascending colon could not be made out, so that the

veins leading from the cecum were exposed with great difficulty. The posterior peritoneum was rich in fat, so that the exposure was made still more difficult. The mesentery of the lower ileum and the peritoneum of the ileocecal angle with the vessels lying behind it were ligated obliquely in several bundles. The transverse incision in the abdominal wall was sutured and abundant drainage provided. The chills which had been present before the second operation were after it repeated several times and they then ceased. The fear of a diffuse peritonitis was not realized and the abdomen remained soft and painless. There developed, however, a fecal fistula, with irregular temperature, slight jaundice, and the clinical picture of general sepsis, from which the patient died three weeks after the second operation. The autopsy showed, together with the localized focus of infection and the fecal fistula of the lower end of the ileum, a thrombophlebitis of the superior and inferior mesenteric veins, portal thrombosis with extension into the finest branches of the portal vein, numerous abscesses in the liver, enlargement of the spleen, and myocarditis.

Making a New Circulation for an Obstructed Circulation in the Abdomen and Lower Extremities.—LANZ (*Zentralbl. f. Chir.*, 1911, xxxviii, 3) says that the cases of elephantiasis which occur in his practice result usually from repeated attacks of erysipelas, in which phlebitis and lymphangitis lead to an inflammatory obstruction of the lymph vessels or from the obstruction of the lymph due to the removal of lymph nodes by operation. In most of them a transitory œdema develops, but in some the lymph stasis becomes permanent and is accompanied by thickening of the subcutaneous tissue. In a troublesome case, after a trial of ten days elevation of the right leg without much success, Lanz made an incision on the outer side of the thigh in its whole length, dividing the fascia lata and exposing the bone behind the posterior edge of the vastus externus muscle. After separating the periosteum from the bone, three openings were made into the medulla, in the upper, middle, and lower thirds of the femur. Narrow strips of fascia lata were then excised, which were introduced into the bone openings, with the hope that along them a collateral circulation of the lymph would develop. The fascial wound was then closed by a suture and many small openings made in the fascia with scissors to favor the escape of the lymph. The skin wound was closed and a collodion dressing applied. The patient left the hospital a few weeks with the wound healed. A year later he reported for examination, when the wound was still healed. Three years after operation examination showed the following result: While before the operation he was compelled from time to time to stop work for three hours and lie down, immediately after the operation he began to improve, and at the present time he can work all day without difficulty. He was examined about four o'clock in the afternoon after working all day, and on inspection there was no important difference in the size of the two limbs. Lanz has had no further opportunity in the last five years to operate again in elephantiasis.

Operative Mobilization of the Upper Jaw in Cleft Palate.—CODIVILLA (*Zentralbl. f. Chir.*, 1911, xxxviii, 105) reports the case of a boy,

aged five years, with a double harelip and a cleft palate involving the hard and soft palate, which was so wide that the fissure in the alveolar process admitted easily two fingers. Without a preliminary operation on the skeleton, sufficient flaps could not be obtained from the cheeks to unite them in the median line except under very severe tension. The usual methods of closing the cleft in the bone could not be employed. While on the left side the bone appeared to have its normal direction and relations to the dental arch, on the right side the superior maxilla was displaced upward and outward, so that the buccal surface was somewhat cone-shaped, with its apex at the basilar bone. Codivilla concluded that the gap could be closed and the abnormal position of the superior maxilla corrected only by mobilization of the latter. A preliminary ligation of the external carotid was performed. Through a small incision in the cheek over the articulation between the superior maxilla and malar bones, this union was separated and the anterior wall of the former divided. On the buccal side the union between the maxilla and the pterygoid process was also divided. By strong pressure with the thumb the alveolar process could be brought close to the intermaxillary bone and thus the nasobuccal gap closed. The abnormal position of the maxilla was also corrected by force and fixed in its new position to the opposite bone by a metallic ligature. In the mouth the fixation was aided by a plate in the roof of the mouth fixed to the teeth on both sides. This apparatus was kept in place for six months without any considerable difficulty and was then removed. The bone was now firmly united and the correction of the deformity excellent. With the aid of a plastic operation on the cheek, the harelip was then closed. Codivilla says that this is the first case in which the maxillæ have been approximated by open operation in cleft palate. Several years after operation the correction of the deformity was still maintained and there was no disturbance in the growth of the teeth.

Anesthesia by the Intratracheal Insufflation of Air and Ether. A Description of the Technique of the Method and of a Portable Apparatus for Use in Man.—Elsberg (*Annals of Surgery*, liii, 161) describes a portable apparatus for the employment of the Meltzer-Auer intratracheal method of inducing general anesthesia in man. In all but one of the cases the anesthesia was complete, the patients being quiet, their muscles relaxed, and the breathing quiet and superficial. In many but not in all of the patients the respiratory movements ceased altogether when the pressure of the air passing into the trachea was so raised that the manometer registered 30 to 40 mm., and apnœa ensued. If the tracheal tube is of the correct size and in proper position, the face of the patient will be of a pink color, with the veins of the forehead slightly prominent. The pulse is full, bounding, and regular. It is possible to keep a patient under primary anesthesia a long period of time if the proper percentage of ether is given with the air. Several of the patients had sensitive corneas during the operation, but they were relaxed and gave no evidence of pain. They were almost fully awake as soon as the insufflation was stopped. There is an entire absence of mucus rattling in the throat during the entire operation. None of the cases had any cough or expectoration at any time, and none had any pulmonary complication of even the mildest kind after the operation.

Uniformly there was no complaint of a feeling of discomfort in the region of the larynx after operation and there was no postoperative vomiting. About 30 patients have been anesthetized by this method, some for intrathoracic disease, many for abdominal or other affections. It has been found very useful in operations about the head and neck, as the anesthetist was never in the operative field or in the way of the operator or his assistants.

THERAPEUTICS.

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

Salvarsan in Syphilis.—WEILER (*Münch. med. Woch.*, 1910, lvii, 2622) has treated 206 cases of syphilis with salvarsan. Forty of these have been under observation for some time, and a recurrence has been observed in 14. Three of these cases have shown symptoms referable to the cranial nerves. Weiler says that it is impossible to interpret these as results of the medication or as syphilitic manifestations. In another case hemorrhagic nephritis developed a few weeks after the injection. Weiler believes that salvarsan has a more rapid action than the usual antisyphilitic remedies in most cases, but that as yet its permanent results are not fully established.

Experimental Studies of the Lethal Dose of Salvarsan in Acid Solution.—HERING (*Münch. med. Woch.*, 1910, lvii, 2621) relates his experiments with the injection of salvarsan in dogs and rabbits. He found that the lethal dose of the acid solution in 0.5 per cent. strength was from 0.004 gram to 0.005 gram per kilo for rabbits and from 0.01 to 0.02 gram for dogs. This makes the lethal dose for a man weighing 150 pounds 0.315 gram if based upon the results in the rabbits, or 1.05 gram if based upon the lethal dose for dogs. Hering believes that the acid reaction is mainly responsible for the toxicity, as he found that the rabbits would survive twenty times the fatal dose and dogs ten times if the drug were given in an alkaline solution.

Atropine Cure in Ulcer of the Stomach, and other Indications for Atropine in Internal Medicine.—SCHICK (*Wiener. klin. Woch.*, 1910, xxiii, 1229) believes that good results are obtained by the use of atropine in the treatment of gastric ulcer. The subjective symptoms, especially pain, disappear quickly after beginning the treatment. Hyperacidity and hypersecretion were less quickly influenced. Pyloric stenosis due to cicatrical contraction was either not at all or only slightly influenced. Schick agrees with the view of Eissinger and Hess that many ulcer cases are dependent upon an increased vagus tone. This increased vagus tone stimulates the gastric secretion as well as the gastric mus-

culature, and can be diminished by a systematic use of atropine. He mentions a long list of conditions benefited by this drug. Among these are spastic constipation, bronchial asthma, excessive sweating, nervous hypersecretion, lead colic, membranous colitis, in certain cases of intestinal obstruction, in cardiospasm, in spasms in œsophageal carcinomata, in gallstone, and renal colic.

The Prevention of Typhoid Fever with Antityphoid Vaccine.—RUSSELL (*Boston Med. and Surg. Journ.*, 1911, clxiv) says that vaccination is a simple and harmless procedure and wherever used has reduced the incidence and mortality of typhoid. The immunization of every individual in the army is perfectly feasible, and it offers the greatest hope of freedom from this plague in the future. Antityphoid vaccine has long since passed the experimental stage. Since 1904, 60,000 men have been vaccinated in India, over 7000 in Southwest Africa, and over 14,000 in the United States. In no case has any harm followed its administration.

The New Preparation of Albumin, "Riba."—VON NOORDEN (*Berlin. klin. Woch.*, 1910, xlvii, 1919) reports that a new preparation of albumin has been perfected after a year's experiment. This is sold under the name "Riba." It is derived from fish and in composition consists principally of albumoses. The preparation is easily soluble in water and is well borne by the digestive tract, and because of its ease of absorption it is of great value in nutrient enemata. It has no unpleasant taste and may be combined with other articles of food. It is a most valuable addition to soups and broths to increase their nutritive qualities. The indications for its use are those of other albumin preparations. Von Noorden particularly advises its use in anemic conditions because he believes they require extra protein nourishment. Riba also has, according to von Noorden, a low purin content, and so is of value in the dietary of gouty patients. Von Noorden states that as much as 110 grams a day of this preparation can be utilized by the body.

Subcutaneous and Intravenous Feeding with Glucose.—KAUSCH (*Deut. med. Woch.*, 1911, xxxvii, 8) advocates the administration of grape sugar solutions by intravenous infusion or by subcutaneous injection in certain conditions that are complicated with persistent vomiting or the loss of great amounts of fluid by the intestinal tract, and that consequently are difficult to feed by ordinary methods. Kausch begins with 1000 cm. of a 2 per cent. solution of glucose for subcutaneous injections, and gradually increases the strength to 5 per cent. He has found that the injection intravenously of 1000 cm. of a 5 per cent. to a 7 per cent. solution is a perfectly harmless procedure. There is no excretion of sugar for several days, and after this period only a small proportion of the glucose is lost by excretion through the kidneys. Kausch found that when the percentage of glucose in the solution was higher than 7 per cent. a glycosuria occurred soon after infusion. However, the amount of sugar excreted was only slight compared to the amount infused. The grape sugar solutions were made in physiological salt solution, and when injected intravenously from

from 4 to 8 drops of a 1 to 1000 adrenalin solution were added. The infusions were much preferred by the patients to the subcutaneous injections. Kausch says that undoubtedly some of the benefits derived were from the saline infusion alone, but that the sugar disappeared and therefore must have oxidized. An amount of extra nutriment up to 500 calories is obtained by this method and this must result in some protection to the body proteins. Kausch relates the history of certain cases of inanition who improved or recovered after these glucose infusions.

Sabromin in Chorea.—MAETZKE (*Deut. med. Woch.*, 1910, xxvi, 1412) reports a single case of chorea favorably influenced by sabromin that had resisted other methods of treatment. The patient received from 3 to 6 tablets daily for a period of three months and also during this time was kept on a strict vegetarian diet.

Experimental and Clinical Observations of the Action of Salvarsan on the Eye.—IGERSHEIMER (*Münch. med. Woch.*, 1910, lvii, 2673) relates his experiments on animals that, according to him, show that salvarsan is non-toxic to the optic nerve. He believes that the toxic action of atoxyl upon the optic nerve is due to phenylarsenate derived from the remedy. He says that salvarsan does not seem to contain phenylarsenate derivatives. He states that cats and dogs are particularly liable to have optic atrophy as a result of the administration of atoxyl, but in his experiments he could find no evidence of any such toxic action upon the optic nerve after the injection of salvarsan. However he did find arsenic in the eyeball after injection of salvarsan. He believes that caution should be used in the administration of the drug for long periods because of this fact, although he does not believe that an arsenical derivative that is toxic for nerve tissue can be split off from salvarsan. He also cites a number of clinical cases in his experience when salvarsan had a curative effect upon syphilitic eye affections.

Antityphoid Inoculation.—RICHARDSON and SPOONER (*Boston Med. and Surg. Journ.*, 1911, clxiv, 8) report 1588 inoculations upon 405 nurses in various training schools for nurses in Massachusetts. As yet there have been no untoward results, and they believe that the inoculated individulas have acquired an increased resistance to typhoid fever that will last for several years at least. They expect in the coming year to extend the influence of these inoculations, especially among nurses and those attendant upon the sick. Furthermore, they have strong faith that the procedure will, within a short time, find increasing favor with the general public, which, exposed as it is to many sources of infection, is in great need of specific protection.

The Effect of Salvarsan upon Cranial Nerves.—EHRLICH (*Berlin. klin. Woch.*, 1910, xlvii, 2346) in this article replies to recent communications regarding supposedly toxic effects upon the cranial nerves as a result of salvarsan therapy. He says that of about 30,000 cases that have been treated with salvarsan, there has been only one undoubted case of optic atrophy occurring in a previously healthy eye after the injection. He goes on to say that this occurred in a case of tertiary

syphilis that had previously been treated with arsacetin and enesol, and he believes it to be more than probable that the optic atrophy was produced by these preparations of arsenic. A few cases of temporarily disturbed hearing have been reported, and also evidences of facial involvement have followed the injections. In conclusion, Ehrlich says that these disturbances are not of toxic origin, but are syphilitic manifestations. They are caused by a few isolated spirochetæ remaining after sterilization of the principal mass, and occur likewise after mercurial treatment. The marked clinical symptoms are due to the fact that the cranial nerves are enclosed in bony canals, where they are liable to attacks of syphilitic periostitis. The few spirochetæ remaining are not enough to give rise to a positive Wassermann reaction. Ehrlich emphasizes the importance of the observation that such disturbances disturbances disappear after the salvarsan treatment is resumed.

Treatment of Banti's Disease.—Banti (*Folia Hæmatologica*, 1910, x, 33) bases his article on a careful study of 50 cases of the disease known clinically as Banti's disease, cases that were definitely proved either by autopsy or operation. He divides the disease into three distinct periods. The first period of the disease may last from three to five years, and even as long as twelve years. This period is characterized by the gradual enlargement of the spleen. Less constant, often only slight or occurring late in the disease is the anemia. The anemia is secondary in type, usually with leucopenia with a relative and absolute lymphocytosis. Banti calls especial attention to cases of this type that an operation or autopsy have proved to be free from liver involvement. The second type of cases comprises those with evidence of a beginning congestion of the portal system. This stage of the disease may last for several years. Finally the third stage consists of those cases with symptoms of cirrhosis of the liver associated with a diminution in size of the liver and the appearance of ascites. Banti advances the theory that the disease may be caused by some infectious agent, possibly of bacterial origin, that first causes the characteristic disease of the fibrous tissue of the spleen reticulum, and then there follows the degenerative changes in the follicle and pulp. He attributes the anemia and general weakness to some toxin produced in the spleen, and also to this same cause the subsequent changes in the liver. Banti advocates early extirpation of the spleen as a cure for this disease. He thinks that if this is done in the first stage a large majority of the cases can be cured. If cases are operated upon in the second stage, the beginning cirrhosis of the liver may be arrested. Banti relates the results in 36 cases operated upon. Of 4 patients operated upon in the first stage, 3 were apparently cured after periods of observation during fifteen, six, and five years. Of 22 cases operated upon during the second period, there were 13 cures, some persisting for fourteen, seven, and eight years. There were 4 cures in 10 patients operated upon during the third stage. Banti says that in late operations it is often impossible to remove the spleen and that then splenoplexy and a modified Talma operation is indicated.

PEDIATRICS.

UNDER THE CHARGE OF
LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,
OF PHILADELPHIA.

Serum Treatment in Diphtheria.—E. W. GOODALL (*Brit. med. Jour.*, 1911, No. 2615, 292) while regarding antitoxic serum as a specific, believes there are certain limits to its use. While he believes in the importance of early treatment, he has modified his earlier view that the limit of its use is the limit of dosage. After the introduction of this serum, and later the sera for tetanus, the streptococcus, and enteric fever, a symptom complex was found to occur after serum injections in a number of cases. This has been called "serum sickness," and has been found to be due to the serum itself and occurs in about 33 per cent. of the cases treated. The general symptoms are fever and a rash, usually urticarial in nature. Other and more severe symptoms were observed in 3 to 4 per cent. of the cases, namely, acute pain and swelling of the joints, pain in the tendons and fasciæ. These general symptoms rarely set in before one week after the serum injection, and sometimes three weeks. The fever, rash, and occasional arthritic symptoms are known as the "normal reaction," and are due to the horse serum. It is known that the sera of other animals can give rise to the same effects. In the great majority of cases the normal reaction, while unpleasant, is not dangerous. "Abnormal reactions" were next recognized and divided into those following a second injection of serum, and those following a primary injection. Abnormal reactions following a second injection have the usual incubation period of at least one week. This reaction is unusually severe and abrupt. There is faintness and much swelling of the body surface and the mucous membranes from the urticaria. A second type of this class exhibits an incubation period shorter than usual, from twelve hours to six days. This is termed "accelerated reaction" and exhibits severe urticarial swelling, vomiting, prostration, and swelling of the joints. In a third type of this group, called "immediate reaction," the serum reaction appears within a few minutes to five or six hours after the injection, and exhibits an explosive suddenness, high temperature, cyanosis, and rigor. From these facts, therefore, it is deduced that in certain persons injection of a foreign serum leads to increased susceptibility to that serum if repeated. "Abnormal reactions" following a first injection are more severe and often fatal. Gillette collected 30 cases of this kind, 16 of which were fatal. Most of them occurred in the United States. Twenty-two in this series were subject to asthma of some form or other. The symptoms of this class of cases are usually intense dyspnœa, failing respiration, with cyanosis and collapse. They occur shortly after the injection. Goodall believes that an indiscriminate use of the serum as a prophylactic is unjustifiable. A delay of a day or two in doubtful cases not laryngeal is justifiable. In undoubted diphtheria Goodall would hesitate to give the serum only when the patient is asthmatic. If the

disease is severe or the larynx is involved, the choice between the two evils would be to give the serum and risk the possible hypersensitiveness. The earlier the treatment in any case, the smaller the dose necessary. Large doses of calcium lactate tend to mitigate the rash of serum sickness.

Chorea Successfully Treated with Salvarsan.—JOHANN V. BOKAY (*Deutsch. med. Woch.*, 1911, xxvii, 111) reports a case of chorea in a child, aged eight years, which was treated with salvarsan. The chorea was so severe that the child was kept in a padded crib to avoid injuring itself. On November 9, 20 grams of salvarsan was injected subcutaneously and was well taken. On November 11 there was a perceptible diminution in the choreiform movements, and a small, painless, infiltrated area was found at the point of injection. On November 14 a marked improvement in the incoördination was observed and a small, centrally placed area of skin necrosis developed on the infiltrated area. On November 23 the choreiform movements were disappearing rapidly. On November 30 the choreic movements were barely perceptible and the child was up and about. By December 8 the patient was entirely cured and the infiltrated area absorbing. A control case of the same age, but with a less marked chorea, was treated at the same time with Fowler's solution of arsenic, beginning November 9, but by December 12 this case still showed marked choreiform movements, although having had a thorough course of the Fowler's Solution. In the first case, except the infiltration and necrosis at the point of injection, no bad effects were observed from the salvarsan. Bokay does not comment on the quick improvement in his case, but remarks that Rumpel found no improvement in chronic articular rheumatism treated with salvarsan.

Neurasthenia in Children.—CLIVE RIVIERE (*The Practitioner*, 1911, lxxxvi, 38) says that standard examples of neurasthenia are found in older boys and girls, and that slighter forms are common in quite early years, childhood supplying the material out of which adult neurasthenics are made. The preneurasthenic child is usually neurotic, and characterized by overdevelopment of the emotional faculties. An unemotional type marks the other end of the scale, and all grades exist between the two types. The neurotic type presents hypersensitiveness, excitability, emotionability, and timidity. The restrained emotional type is gloomy, solitary, shy, and may be thought dull. The neurotic child is prone to suffer from the functional neuroses, such as night terrors, "tics," and chorea, migraine, epilepsy, asthma, etc., and is peculiarly subject to acute rheumatism. In young children a deficiency of nerve force may be present from earliest childhood, and is characterized by weakness, weariness, poor concentration, and abnormal sensitiveness to climatic conditions. The digestion is weak and capricious, nutrition subnormal, and the hands and feet are habitually cold. The opposite type is the starved neurasthenic, produced by poverty, underfeeding, and loss of sleep, and is characterized by pallor, apathy, and chronic exhaustion. A third type exhibits gastro-intestinal dyspepsia or "mucous disease," combined with neurasthenic symptoms. Treatment of the gastro-intestinal tract does not altogether cure,

where a want of nerve force is primarily responsible. Splanchnic vasomotor paresis, a "pooling" of blood in the splanchnic area, is a marked phenomenon in many cases, and is largely responsible for the feeble circulation, pallor, tendency to faints, and probably intestinal symptoms, including the mucous flux. The treatment of neurasthenia in childhood should be preventive. A non-stimulating, quiet, uneventful childhood is essential. The masticatory instinct must be thoroughly educated to avoid dyspeptic troubles. Schooling is essential, and large public schools are not to be recommended. Underlying causal conditions should be sought and removed; among these are excessive school strain and malnutrition, and overfeeding or "stuffing," especially with sweet carbohydrate "slops." The latter requires a regulated dietary, in a dry form thoroughly masticated, and dietary discipline. Tendency to splanchnic congestion requires special treatment. The feet and legs, if cold, are rubbed and well covered. Daily recumbency for an hour or so is of value. Exercises to strengthen respiratory and abdominal muscles, and a cold sponge or spinal douche are important. Among drugs, occasional use of calomel is valuable. Malt extract and pancreatin are also of value, and digitalis in many cases tends to brace up splanchnic circulation.

Some Points on "Serum Disease."—Johann v. Bokay (*Deutsch. med. Woch.*, 1911, xxxvii, 9), in connection with the injurious effects of serum injections, approves of the term "serum sickness," applied to this condition by v. Pirquet and Shick, who described it as a definite clinical picture. Besides the skin affections are found fever, pain, and swelling in the joints, localized œdema, and albuminuria. Instances of this condition since 1894 indicate that the first signs of this condition appear from eight to ten days after the injection of the serum. However, some cases arise in which these reactions to serum occur much more rapidly, even immediately after the injection. Von Pirquet, Shick, and others have shown that this "accelerated reaction" occurs usually where a condition of "anaphylaxis" exists. There is no doubt that anaphylaxis often causes unpleasant symptoms, and the possibility of serum sickness should always be considered at the bedside when, after an interval, serum injection is again necessary. This is especially true, since all these sera are derived from the horse. Wolff-Eisner has indicated the elimination of anaphylaxis by using serum from another species of animal. Bokay thinks it would be wise if, in the future, diphtheria antitoxin were prepared not only from the horse, but from other animals, as the sheep, cow, and ass. The "accelerated reaction" to serum, Bokay thinks, indicates a previous inoculation of the patient with serum from the same species. He reports 2 cases of diphtheria in children of different families. Neither child had ever had any serum injection. They were both injected with the same quantity of a serum which was prepared at the same time from the same horse. Within a few minutes after the injection, both children broke out in a severe urticarial eruption, covering the face and scattered over the body. This rash faded within a day. These cases cannot be explained on the ground of anaphylaxis. In 1908 about 10 per cent. of cases occurring in Bokay's observation developed serum sickness, and in 1909 there was 23 per cent. In the month of January, 1911, out of 23 cases, 50

per cent. developed a serum exanthem. In all these cases the disease appeared as usual about eight or ten days after the injection. The serum used for these cases came from one lot derived from the same horse. Bokay thinks the cause of the serum sickness in the two children above described was due to some individual element of the horse from which the serum was derived.

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Cesarean Section for Impassable Contraction Ring.—DICKINSON (*Surg. Gyn. and Obstet.*, October, 1910) reports the case of a patient who, in her first labor, had a contraction ring obstruction to delivery which necessitated the use of forceps, followed by the loss of the child. The patient was delivered at the thirty-second week, the obstructing ring did not relax under chloroform, and the death of the child was due to the compression necessitated by delivery. Two years later the patient again came into labor, with pains every half hour for forty-eight hours. The cervix was soft, the membrane detached, the character of the contractions good, the head remaining high, with the occiput posteriorly and the back to the left. A contraction ring of the thickness of the thumb, admitting two fingers, lay just above the pelvic brim two inches beyond the softened cervix, and surrounding the entire circumference of the uterus. No internal os, apart from this upper circle, could be located. The lower segment was relaxed but was not thinned. Morphine, and attempts at dilatation under surgical anesthesia, failed, and uterine contraction was constant, but with each active pain the contraction ring hardened perceptibly. The membranes had ruptured a few hours previously, and the general condition of the mother and child was good. As the parents were desirous of obtaining a living child, section was chosen and was successful. The ring retained its contraction after the emptying of the uterus.

Dickinson also reports an operation in a primipara for a similar condition, which was successful. Two cases operated upon by Watt are also reported. In the first of these, two attempts had been made to deliver with forceps, but the writer believed, as aseptic precautions had been employed, that these attempts had not seriously jeopardized the results of the Cesarean operation. Section was accordingly performed. The mother died of septic peritonitis on the ninth day, but the child survived. The second case was a primipara of more than usual muscular development, upon whom delivery with forceps was tried with negative results. On admission to hospital the occiput was found posteriorly, and the forceps was again tried; this attempt was repeated but without success. Section was performed, the mother dying twelve hours after operation, but the child survived.

Dickinson collected 6 cases of section, reported in the literature of the subject, done for contraction ring; 3 of the 6 mothers died; two children survived—the two that were living when the operation was undertaken. One of the mothers who died was an eclamptic; in the case of the other two, the operation had been delayed and the patients had been subjected to previous efforts at delivery. In some of the more desperate cases reported, hysterectomy was successful. Dickinson believes that the contraction ring is the lower edge of the muscle of the body of the parturient uterus in action. It makes no clinical difference whether the ring is an anatomical internal os or not. Its presence is a physiological occurrence, resulting from normal activity, which is in excess, or from unbalanced development, and in either case it may constitute a slight or serious obstacle to delivery. In its least degree it is physiological and gradually disappears as the fœtus passes out of the uterus. In a greater degree, it is an hour-glass narrowing in the later stages of labor, its tension and resistance increasing during each pain. The body of the uterus shortens and thickens throughout its entire wall. In its most pronounced development, it is a part of tetanus of the uterus developing late in labor. The ring either retains the fœtus in the uterine body, leaving the lower uterine segment empty, or encircles part of the fœtus, usually the neck, the head moving in the lower segment. When fully developed, it may be palpated externally as it rises in the abdomen, or may be determined by vaginal examination. One-third of the mothers and one-half of the children died in the reported cases. The most important factor affecting mortality is early recognition of the complication. As the obstruction is more distant from the exit than any other whatever, it demands an operation, which can safely be performed from above. If the child be dead, the spasm can usually be relaxed by morphine and complete ether narcosis, and the child removed by vaginal procedure. In some cases even embryotomy and basiotripsy have failed to empty the uterus, and in fear of septic infection, hysterectomy was performed. In a case not infected with a dead fœtus retained behind an undilatable ring admitting but two fingers from above the pelvic inlet, Cesarean section should be performed, and not embryotomy, if the patient can have hospital care. If the child be living, a persistent effort should be made to dilate the ring by rest, morphine, surgical anesthesia under ether, and patient manual dilatation. In head cases, a fair essay of forceps, short of the risk of cerebral hemorrhage, and combined with expression, is undertaken. In transverse cases, version should be attempted, bearing in mind the risk of rupture. If the forceps fail in head cases, and version cannot be performed in transverse, the fœtal heart being good and the cord unharmed, choice is made between embryotomy and section. Embryotomy will usually be chosen because of the frequency of lowered vitality in the child, when accessibility favors this operation, and because of the lessened risk to the mothers in most instances. With mother and child in fair condition, with infection unlikely, with a ring not yielding to a combination of morphine, etherization, and manual dilatation and contraction, Cesarean section is indicated in preference to embryotomy, and should be undertaken if the parents elect a somewhat increased risk for the sake of the child. Cesarean section is safer

than embryotomy in the worst degrees of ring contracture and tetany located high, provided infection is improbable.

[The reviewer would call attention to these cases as illustrating a fact which he believes is being constantly demonstrated in obstetric practice. It will be observed that in this report of cases those in which forceps or version had been tried necessitated hysterectomy, or without this, died from infection. Increasing experience confirms the reviewer in the belief that the application of forceps or attempts at version makes the performance of the conservative Cesarean section unjustifiable. No matter how careful the operator may be in his personal asepsis, such manipulation carries into the uterus bacteria from the vagina, which become pathogenic, and traumatisms are inevitable in these manipulations. The decision to perform Cesarean section should be made before resorting to forceps, version, or manual dilatation. In these cases there is no necessity for manual dilatation if section is to be performed, as there is sufficient dilatation to permit the drainage of the lochial discharge. If attempts at version or forceps or manual dilatation have been made and have failed, and Cesarean section is to be performed, hysterectomy is indicated. Such cases are preëminently hospital cases, and are more dangerous than pelvic contraction, because the obstacle to delivery is not apparent.—E. P. D.]

Cesarean Section under Local Anesthesia.—SMITH and SCHWARZ (*Surg., Gyn., and Obstet.*, October, 1910) report 2 cases of Cesarean section under local anesthesia. The first was that of a primipara having a kyphotic and scoliotic spine, mitral regurgitation, chronic nephritis, and a funnel-shaped, generally contracted pelvis. The second case had a generally contracted pelvis, showing some traces of rachitis. The patients agreed to local anesthesia, with the understanding that should pain be felt, gas and oxygen were to be administered. The solution used was ½ per cent. of novocain in normal salt solution, to each 10 c.c. of which was added one drop of 1 to 1000 adrenalin solution. This was freshly made and boiled for five minutes, just before using. Two points, one 9 cm. above the umbilicus, and the other a like distance below it in the median line, were infiltrated with a drop of the solution, and from these, as points of departure, the solution was injected about a diamond-shaped area subcutaneously, and then subfascially. The line of the incison was not infiltrated in either of these cases. The amount of the solution used was about 75 c.c. in one case, and 60 c.c. in the other. The operation was performed by opening the uterus *in situ* and removing the child and placenta. The uterus was then lifted out of the abdominal cavity and surrounded by pads dipped in hot saline solution. In the first case the cervix was dilated by the finger passed through the uterine incision, followed by Goodell's dilator. In both cases there seemed to be absolute absence of pain throughout the operation, notwithstanding the dilatation of the cervix from within the uterus in the first case, and the squeezing of the uterus forcibly in the second case, to see if pain could be produced. There was slight loss of blood, although no ligature was passed about the uterus, nor were the broad ligaments compressed. It is not believed that the local anesthesia had anything to do with this. Neither patient suffered shock, and each had practically a normal convalesence.

GYNECOLOGY.

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA

A New Method of Replacing the Retroflexed Uterus.—GOLDBERG (*Zeit. f. Gyn.*, 1910, xxxiv, 1645) describes the following method which has been useful in his hands. A sharply bent Hodge pessary of the proper size is introduced into the vagina so that the broad end lies firmly against the posterior vaginal fornix. With the palmer surface directed upward, the index and middle fingers of the left hand are introduced between the pessary and the anterior vaginal wall as far as the cervix where the fingers are separated the width of the portio. By means of the dorsal surface of the fingers, pressure is made backward on the anterior small end of the pessary. Gentle abdominal manipulation with the right hand will easily bring the uterus forward. Especially adaptable for this method are those cases of retroflexion associated with relaxation of the uterine ligaments and surrounding tissues. In nullipara with hypoplastic retroverted uteri is reposition impossible by any method; a short portio and flat vaginal fornix render this method unsuitable.

Arteriosclerosis of the Uterine Vessels.—CHALFONT (*Jour. Amer. Med. Assoc.*, 1911, lvi, 239) has made a study of eleven uteri removed on account of repeated hemorrhages unassociated with neoplasm and three uteri from multiparæ presenting a normal menstrual history. He concludes that proper uterine contraction is essential to the control of uterine bleeding. There is no definite pathological condition present in these cases that is not found in others not giving any history of hemorrhage, with the possible exception of the increase in number and size of vessels. Some loss of functional power of the uterine muscle is the predisposing cause of bleeding in cases of arteriosclerosis. This loss of functional power is due either to the development of fibrous and elastic tissue from subinvolution or to the condition which caused this subinvolution. The exciting causes are probably many. Chalfont suggests the increase in size and number of vessels, general increase in blood pressure from kidney disease or general arteriosclerosis, passive congestion from heart disease, local congestions or general muscular weakness.

The Utilization of the Anterior Cervical Wall in the Operation for Vesicovaginal Fistula.—KUSTNER (*Zeit. f. Geb. u. Gyn.*, 1910, lxvii, 603) devotes fifty-two pages to the description of his operative technique for the cure of vesicovaginal fistula and to the analysis of 50 cases which he has operated upon by this method. Briefly summarized, the operation consists in freeing the bladder from the cervix, denuding the vagina around the fistula, and uniting the vaginal cuff to the cervix by interrupted, non-absorbable sutures. This procedure is applicable to any form of vesical fistula, does not sacrifice tissue,

utilizes the anterior cervical wall as a splint, and avoids all risk of injury to the ureters. Of the 50 fistulæ reported, 5 were cervicovesical, 14 cervicovesicovaginal (cervical defects), and 30 vesicovaginal. Primary healing resulted in 46 cases, while 4 required a second operation.

An Experimental Study of Ascending Genital Tuberculosis.—In order to substantiate his previous assertion that genital tuberculosis may be due to an ascending infection, JUNG (*Archiv f. Gyn.*, 1910, xcii. 764) reports the results of his experiments in 33 rabbits. The inoculations of tuberculous material were made either into one uterine horn or into the vagina, under such precautions as would prohibit direct injection into the uterine cavity. In the selection of his specimens for microscopic study, he excluded those which showed peritoneal tubercles, since the objection could be made that the infection had extended from without inward and not by way of the uterine cavity. The author has been able to demonstrate five instances of true ascending tuberculous infection. Careful study of the preparations afforded no evidence of congestion of the uterine secretion which might act as a provocative factor, an assertion which Baumgarten denies. In a supplementary article (page 775) Engelhorn offers further proof of the possibility of an ascending infection. Following the injection of carmine into the vagina, the rabbits were killed at varying intervals and the pigment could be plainly seen in the mucosa, muscularis, or subperitoneal tissue, depending upon the length of time elapsing after the injection. In the human, hematogenous infection is the rule; in rare cases a primary ascending genital tuberculosis undoubtedly exists.

Active Substances in the Uterus and Ovary.—SCHICKELE (*Münch. med. Woch.*, 1911, lviii, 123) has carried out a series of experiments with extracts of the uterus and ovaries in order to determine their action upon the coagulability of the blood. These extracts were obtained by subjecting the organs to high pressure—four to five hundred atmospheres. He has been able to demonstrate conclusively that coagulation is decidedly retarded; this was especially marked with extracts of uteri which had been extirpated on account of profuse hemorrhage from myomata or metrorrhagia associated with no demonstrable lesion when coagulation did not occur in from six to twenty-four hours. While extracts similarly obtained from other glands of internal secretion produced a delay in the coagulation time, this was in no way comparable to the action of the uterine and ovarian substances; extracts from the corpus luteum were especially active, as evidenced by the fact that coagulation did not take place in twelve days. The author also tested the effects of these extracts given intravenously, and found that an intense lowering of blood pressure followed as the result of peripheral dilatation of the bloodvessels, often associated with delay in the coagulation time. Twitchings and even convulsions were often accompanied by partial unconsciousness; with a more intense action, the respirations and pulse became slower, and in some instances death of the animal rapidly ensued.

Some Observations on the Operation of Abdominal Myomectomy for Myomata of the Uterus.—W. J. MAYO (*Surg., Gyn., and Obstet.*,

1911, xii, 97) bases his remarks upon an experience of 1244 operations for uterine myomata. In patients between the ages of twenty and thirty years myomectomy is the operation of choice unless the ovaries are sufficiently diseased to require removal when hysterectomy is indicated; between thirty and forty years, each case must be judged upon its own merits, and the wishes of the patient should be an important factor in deciding upon the type of operation; between forty and fifty years hysteromyomectomy is the wiser procedure. The most serious objection which has been offered against myomectomy is the increased mortality from sepsis and hemorrhage. Care in avoiding undue suture tension will lessen the chances of infection; hemorrhage is best controlled by a continuous catgut suture. Should oozing from the needle puncture follow myomectomy in a pregnant uterus, the tip of the omentum may be used as a pressure pad along the line of suture. Curettement of the uterus through an incision in the anterior wall has been found very useful; in several cases the removal of a polypus which had caused severe hemorrhage, avoided hysterectomy. No fatalities and but one miscarriage followed myomectomy during pregnancy. Only seldom must the uterus be emptied when myomata complicate pregnancy, and hysteromyomectomy with the non-viable child is one of the rarest necessities, because myomectomy usually suffices. At term, in cases where myomata obstruct the pelvic outlet, the Porro operation is indicated. A table of the various operations and results is appended.

Carcinoma of the Uterus.—SCHAUTA (*Med. Klin.*, 1911, vii, 6) mentions the various methods which have been devised for the treatment of carcinoma of the uterus, such as drugs, ferments, cauterization, fulguration, etc., and states that these remedies have at best only a palliative action. The knife offers the only hope of cure. In order to obtain uniform statistics, he has practically limited himself to the vaginal route, and his results compare favorably with the radical abdominal operation of Wertheim. The primary mortality has been reduced from 10 to 4 per cent.; the operability is between 50 and 60 per cent.; 40 to 50 per cent. have been permanently cured, and in his last series of cases the absolute cures will be 28 per cent., four years elapsing since operation. These figures show that even in the most skilled hands only 20 to 25 out of every 100 cancer patients can be cured. How can these results be improved? The acme of technical skill and radical excision has been reached; the only avenue of improvement lies in early diagnosis of the disease and immediate operation. The brunt of responsibility must fall upon the general practioner, to whom the patient usually presents herself first; an examination should be made of all patients who present irregularities during the menopause, in order to rule out cancer. Further, education of the public is necessary; the objection that undue fear will be aroused in the mind of the public is more than offset by the number of lives that will be saved.

Epidural Injections in Sacral Pains.—ALBRECHT (*Zent. f. Gyn.*, 1911, xxxv, 50) has employed epidural injections of normal salt solution in 53 cases of sacral pain unassociated with gross disease of the genitalia. In 38 cases the pain was completely relieved by one injection, while in

15 cases little or no benefit resulted. In most instances various forms of treatment had been used with no benefit. Out of 16 cases of purely functional neurosis, one injection was curative in 9; no improvement followed in 2 cases. Success followed one injection in 3 cases of retroflexion which operation had failed to influence. The sacral pain was completely relieved in 11 out of 13 cases of chronic inflammatory disease of the adnexa and parametria. Two out of 3 cases of eneuresis were cured by one injection. From his observations he concludes that epidural injections of normal salt solution are indicated in those cases of sacral pain where the absence of a demonstrable pelvic lesion makes local or operative treatment useless and where the other usual methods have failed. Further, he recommends the injection for the treatment of functional bladder conditions as well as essential pruritis vulvæ and coccygodinia.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF
WARFIELD T. LONGCOPE, M.D.,
DIRECTOR OF THE AYER CLINICAL LABORATORY, PENNSYLVANIA HOSPITAL, PHILADELPHIA.

The Relative Importance of the Bovine and Human Types of Tubercle Bacilli in the Different Forms of Human Tuberculosis.— PARK and KRUMWIEDE (*Jour. Med. Research*, 1910, xxiii, 205) report the results of an extensive statistical study of 43 strains of tubercle bacilli obtained from unselected cases of tuberculosis in human beings. Most of the material was derived from the New York hospitals. They conclude that tubercle bacilli isolated from man fall into two groups; one of these groups is identical in all its characters with that found in cattle, and consequently they differentiate two groups which have been designated human and bovine types. Each type shows certain differences, the most important for separation being found culturally and in virulence. The great majority of cultures group themselves around two extremes, though there are a few cultures showing variant characteristics. There is no overlapping of the characteristics; these two types are probably different because of residence in different hosts over long periods of time, and as such are stable. Though observations have been recorded to show that a rapid change of type may take place, these experiments are incomplete and inconclusive, and no confirmation of such results could be obtained by the authors. The result of this study showed that of the 436 cultures examined, 403, or something over 90 per cent., were of the human type. Only one culture of bovine type was found in an adult, and that in a case of genito-urinary tuberculosis; 9 cultures of the bovine type out of a total of 54 occurred in children from five to sixteen years of age, and 22 cultures out of a total of 84 occurred in children under five years of age. It may thus be seen that the bovine type of tubercle bacillus occurs most frequently early in life, over 26 per cent. of the cases of tuberculosis in children under five years of age showing

this type of bacillus. The bovine type of bacillus was found most frequently in cervical tuberculous adenitis, though it was also found in abdominal tuberculosis, in generalized tuberculosis of alimentary origin, in generalized tuberculosis, and tuberculous meningitis. These valuable statistics, the largest that have been accumulated by any one writer, added to the collected statistics, give a total of 1042 cases of tuberculosis in which the type of organism has been identified.

The Presence of a Diastatic Ferment in Leukocytes.—It was first shown by Bial in 1892 that the blood and lymph contained a ferment which was capable of digesting starch. Later, this was fully confirmed by others, but there has been much discussion concerning the origin of this enzyme. The theory that it came from the pancreas or from the liver, which was also shown to possess diastatic properties, seemed most probable. HABERLANDT (*Pflüger's Arch.*, 1911, cxxxii, 175) has recently published some investigations which throw very definite light upon, at least, one possible source of the diastatic ferment of the blood. Working at first with cold-blooded animals, he was able to show that the lymph from the lymph sacs of frogs was capable of digesting starch. Different starches, however, showed various grades of susceptibility to this ferment. Amylen, a starch from wheat was most easily affected, whereas the starches from potato and rice were much less readily acted upon. Microscopically the lymph contained a few leukocytes and by studying these cells it was possible to make out that they ingested the starch granules. Later the starch granules underwent dissolution within the protoplasm of the cell. By increasing the number of leukocytes in the lymph the amount of digested material increased. There was, however, always some digestion of the starch granules, even though the lymph was free of cells. The ferment action was therefore not wholly dependent upon the presence of leukocytes. The same ferment was demonstrated in the subcutaneous tissues and tissue juices of rabbits, and here again the action was increased by the presence of leukocytes. It was thought possible that the ferment which was present in the serum, and tissue juices might rise from destruction of cells, and therefore the relative amount of enzyme was estimated in blood plasma in fresh serum and in blood serum which had stood for twenty-four hours in contact with the clot. The proportion of ferment, however, was equal in each instance, and therefore it did not seem probable that the enzymes were liberated to any amount from the leukocytes during the production of the blood clot.

The Action of Diuretics upon Diseased Kidneys.—In a previous article (*Deut. Arch. f. klin. Med.*, 1909, xcviii) HEDINGER and TAKAYASU have shown by means of experimentally induced nephritis that the kidney reacts differently toward certain diuretics, according to the toxic agent which is used to induce the nephritis. Chrome salts, sublimate, and uranium nitrate are toxic agents which attack first the tubular epithelium and leave at first the vessels undamaged. In the early stages of this tubular form of nephritis salt solution and caffeine, when ingested, cause an increase in the volume of the kidney with diuresis. Cantharadin and arsenic, on the other hand, attack primarily the bloodvessels of the kidney and set up a vascular form of nephritis.

In the early stage of this vascular nephritis, neither salt solution nor caffeine produces any increase in the volume of the kidney or diuresis. The ability of a substance to produce diuresis seems, therefore, dependent upon the ability of the bloodvessels of the kidney to react to stimuli. Hedinger (*Deut. Arch. f. klin. Med.*, 1910, c, 305) has now extended these experiments and has studied the diuretic action of other drugs in experimental nephritis, and especially the digitalis derivatives. Recently Jonescu and Loewi have shown that small doses of digitalis have a diuretic effect in normal animals. This does not take place, as was once supposed, through increased heart action, but by a dilatation of the kidney vessels through a direct action of the drug upon the vessels. Hedinger used for his experiments digipuratum, digalen, theophyllen, and sodium chloride. The injections were made intravenously. In the normal rabbit, digipuratum and digalen produced very slight increase in the volume of the kidney and scarcely any appreciable diuresis. Theophyllen caused decided increase in kidney volume with diuresis, while the same effect, though a much more marked one, occurred with sodium chloride. In the early stages of the tubular form of nephritis, caused by chrome salts, both the digitalis derivatives produced increase in kidney volume and much more diuresis than was observed in normal rabbits. Theophylen and sodium chloride acted in the same way. In animals suffering from uranium nephritis the same increase in kidney volume and diuresis was observed in the early stages, but very soon, as the kidney lesion progressed, this disappeared. In the true vascular type of nephritis caused by cantharadin, none of these drugs showed the slightest ability to increase the kidney volume or to cause diuresis. In no instance did any of the drugs cause any change in blood pressure. In the first stages of the tubular form of nephritis the bloodvessels of the kidney respond more readily, therefore, to small doses of digapuratum and digalen than the bloodvessels of the normal kidney, and consequently an active diuresis is set up. Later in the intoxication and when the vessels are severely injured, as in cantharadin nephritis, even the most active diuretics become ineffective.

Notice to Contributors.—All communications intended for insertion in the Original Department of this JOURNAL are received only *with the distinct understanding that they are contributed exclusively to this* JOURNAL.

Contributions from abroad written in a foreign language, if on examination they are found desirable for this JOURNAL, will be translated at its expense.

A limited number of reprints in pamphlet form, if desired, will be furnished to authors, *provided the request for them be written on the manuscript.*

APR

VOL. CX

AN
TH

THE AN
LAR
GEO

ARNETH
PU

SOME E
TH

RESEAR
HIR

THE VA
M.D

THE R
OF

THE C
M.

THE
IN

PULSA

THE D

VACCI

COPYRIG